

Connecting via Winsock to STN

Welcome to STN International! Enter x:X

LOGINID:sssptal626amd

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * Welcome to STN International * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 Apr 08 "Ask CAS" for self-help around the clock
NEWS 3 Apr 09 BEILSTEIN: Reload and Implementation of a New Subject Area
NEWS 4 Apr 09 ZDB will be removed from STN
NEWS 5 Apr 19 US Patent Applications available in IFICDB, IFIPAT, and
IFIUDB
NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and
ZCAPLUS
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 9 Jun 03 New e-mail delivery for search results now available
NEWS 10 Jun 10 MEDLINE Reload
NEWS 11 Jun 10 PCTFULL has been reloaded
NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
NEWS 13 Jul 22 USAN to be reloaded July 28, 2002;
saved answer sets no longer valid
NEWS 14 Jul 29 Enhanced polymer searching in REGISTRY
NEWS 15 Jul 30 NETFIRST to be removed from STN
NEWS 16 Aug 08 CANCERLIT reload
NEWS 17 Aug 08 PHARMAMarketLetter(PHARMAML) - new on STN
NEWS 18 Aug 08 NTIS has been reloaded and enhanced
NEWS 19 Aug 09 JAPIO to be reloaded August 25, 2002
NEWS 20 Aug 19 Aquatic Toxicity Information Retrieval (AQUIRE)
now available on STN
NEWS 21 Aug 19 IFIPAT, IFICDB, and IFIUDB have been reloaded
NEWS 22 Aug 19 The MEDLINE file segment of TOXCENTER has been reloaded

NEWS EXPRESS February 1 CURRENT WINDOWS VERSION IS V6.0d,
CURRENT MACINTOSH VERSION IS V6.0a(ENG) AND V6.0Ja(JP),
AND CURRENT DISCOVER FILE IS DATED 05 FEBRUARY 2002
NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * STN Columbus * * * * *

FILE 'HOME' ENTERED AT 13:21:47 ON 20 AUG 2002

=> fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'REGISTRY' ENTERED AT 13:21:54 ON 20 AUG 2002

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

DICTIONARY FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNnote 27, Searching Properties in the CAS
Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=>

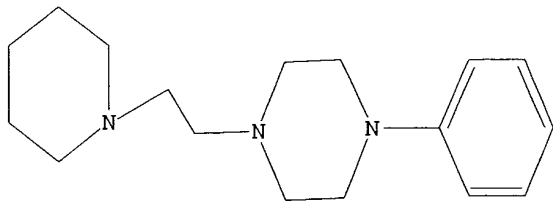
Uploading 09764710.str

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 ful

FULL SEARCH INITIATED 13:22:10 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 6501 TO ITERATE

100.0% PROCESSED 6501 ITERATIONS
SEARCH TIME: 00.00.01

317 ANSWERS

L2 317 SEA SSS FUL L1

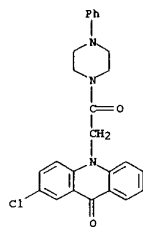
=> s 12 and caplus/lc
23929408 CAPLUS/LC

L3 288 L2 AND CAPLUS/LC

=> s 12 not 13
L4 29 L2 NOT L3

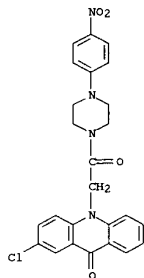
=> d 1-29

L4 ANSWER 1 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 420834-76-0 REGISTRY
 CN Piperazine, 1-[(2-chloro-9-oxo-10(9H)-acridinyl)acetyl]-4-phenyl-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C25 H22 Cl N3 O2
 SR Chemical Library
 LC STN Files: CHEMCATS



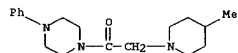
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 2 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 403716-00-7 REGISTRY
 CN Piperazine, 1-[(2-chloro-9-oxo-10(9H)-acridinyl)acetyl]-4-(4-nitrophenyl)-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C25 H21 Cl N4 O4
 SR Chemical Library
 LC STN Files: CHEMCATS



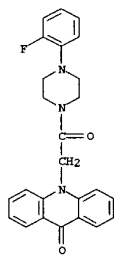
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 3 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 397880-89-6 REGISTRY
 CN Piperazine, 1-[(4-methyl-1-piperidinyl)acetyl]-4-phenyl- (9CI) (CA
 INDEX NAME)
 FS 3D CONCORD
 MF C18 H27 N3 O
 SR Chemical Library
 LC STN Files: CHEMCATS



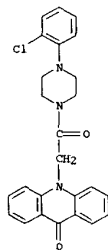
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 4 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 389577-94-0 REGISTRY
 CN Piperazine, 1-(2-fluorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C25 H22 F N3 O2
 SR Chemical Library
 LC STN Files: CHEMCATS



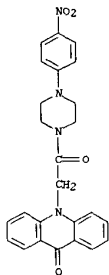
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 5 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 389577-90-6 REGISTRY
 CN Piperazine, 1-(2-chlorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-
 (9CI)
 (CA INDEX NAME)
 FS 3D CONCORD
 MF C25 H22 Cl N3 O2
 SR Chemical Library
 LC STN Files: CHEMCATS



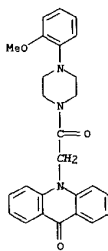
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 6 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 389577-88-2 REGISTRY
 CN Piperazine, 1-(4-nitrophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-
 (9CI)
 (CA INDEX NAME)
 FS 3D CONCORD
 MF C25 H22 N4 O4
 SR Chemical Library
 LC STN Files: CHEMCATS



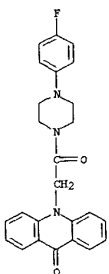
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 7 OF 29 REGISTRY COPYRIGHT 2002 ACS
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 (9CI)
 (CA INDEX NAME)
 FS 3D CONCORD
 MF C26 H25 N3 O3
 SR Chemical Library
 LC STN Files: CHEMCATS



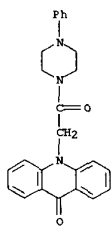
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 8 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 389577-29-1 REGISTRY
 CN Piperazine, 1-(4-fluorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-
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 (CA INDEX NAME)
 FS 3D CONCORD
 MF C25 H22 F N3 O2
 SR Chemical Library
 LC STN Files: CHEMCATS



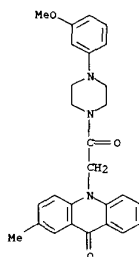
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 9 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 389577-27-9 REGISTRY
 CN Piperazine, 1-[(9-oxo-10(9H)-acridinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C25 H23 N3 O2
 SR Chemical Library
 LC STN Files: CHEMCATS



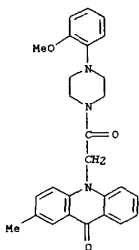
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 10 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 362494-03-9 REGISTRY
 CN Piperazine, 1-(3-methoxyphenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C27 H27 N3 O3
 SR Chemical Library
 LC STN Files: CHEMCATS



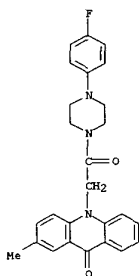
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 11 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 362493-98-9 REGISTRY
 CN Piperazine, 1-(2-methoxyphenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C27 H27 N3 O3
 SR Chemical Library
 LC STN Files: CHEMCATS



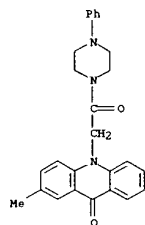
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 12 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 362493-85-4 REGISTRY
 CN Piperazine, 1-(4-fluorophenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C26 H24 F N3 O2
 SR Chemical Library
 LC STN Files: CHEMCATS



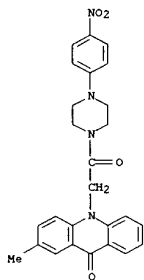
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 13 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 362493-56-9 REGISTRY
 CN Piperazine, 1-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-4-phenyl-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C26 H25 N3 O2
 SR Chemical Library
 LC STN Files: CHEMCATS



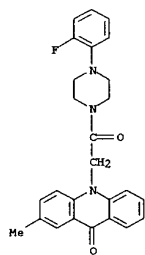
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 14 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 362493-55-8 REGISTRY
 CN Piperazine, 1-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-4-(4-nitrophenyl)-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C26 H24 N4 O4
 SR Chemical Library
 LC STN Files: CHEMCATS



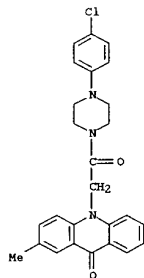
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 15 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 362493-49-0 REGISTRY
 CN Piperazine, 1-(2-fluorophenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C26 H24 F N3 O2
 SR Chemical Library
 LC STN Files: CHEMCATS



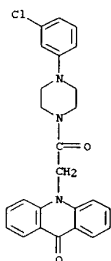
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 16 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 361197-24-2 REGISTRY
 CN Piperazine, 1-(4-chlorophenyl)-4-[(2-methyl-9-oxo-10(9H)-acridinyl)acetyl]-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C26 H24 Cl N3 O2
 SR Chemical Library
 LC STN Files: CHEMCATS



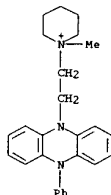
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 17 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 361188-24-1 REGISTRY
 CN Piperazine, 1-(3-chlorophenyl)-4-[(9-oxo-10(9H)-acridinyl)acetyl]-
 (9CI)
 (CA INDEX NAME)
 FS 3D CONCORD
 MF C25 H22 Cl N3 O2
 SR Chemical Library
 LC STN Files: CHEMCATS

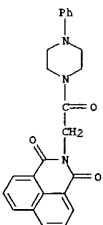


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 18 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 342603-26-3 REGISTRY
 CN Piperidinium, 1-methyl-1-[2-(10-phenyl-5(10H)-phenazinyl)ethyl]- (9CI)
 (CA INDEX NAME)
 FS 3D CONCORD
 MF C26 H30 N3
 CI C04
 SR CA

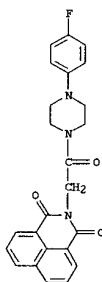


L4 ANSWER 19 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 326889-78-5 REGISTRY
 CN Piperazine, 1-[(1,3-dioxo-1H-benz[de]isoquinolin-2(3H)-yl)acetyl]-4-phenyl-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C24 H21 N3 O3
 SR Chemical Library
 LC STN Files: CHEMCATS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

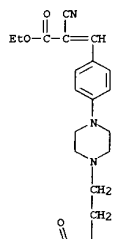
L4 ANSWER 20 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 326889-59-2 REGISTRY
 CN Piperazine, 1-[(1,3-dioxo-1H-benz[de]isoquinolin-2(3H)-yl)acetyl]-4-(4-fluorophenyl)- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C24 H20 F N3 O3
 SR Chemical Library
 LC STN Files: CHEMCATS



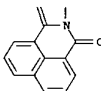
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 21 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 324774-78-9 REGISTRY
 CN 2-Propenoic acid,
 2-cyano-3-[4-[4-[2-[(1,3-dioxo-1H-benz[de]isoquinolin-2(3H)-yl)ethyl]-1-piperazinyl]phenyl]-, ethyl ester (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C10 H28 N4 O4
 SR Chemical Library
 LC STN Files: CHEMCATS

PAGE 1-A

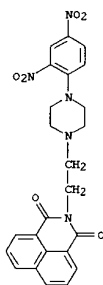


PAGE 2-A



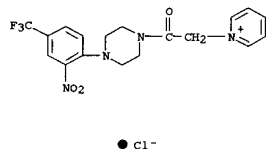
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 22 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 309735-93-1 REGISTRY
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2,4-dinitrophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C24 H21 N5 O6
 SR Chemical Library
 LC STN Files: CHEMCATS



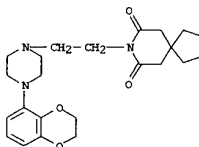
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 23 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 219139-24-9 REGISTRY
 CN Pyridinium,
 1-[2-[4-[2-nitro-4-(trifluoromethyl)phenyl]-1-piperazinyl]-2-oxoethyl]-, chloride (9CI) (CA INDEX NAME)
 MF C18 H18 F3 N4 O3 · Cl
 SR CAS Registry Services
 LC STN Files: CHEMCATS



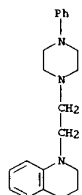
● Cl⁻

L4 ANSWER 24 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 171877-12-6 REGISTRY
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C23 H31 N3 O4
 CI COM
 SR CA



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

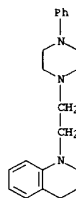
L4 ANSWER 25 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 112991-17-0 REGISTRY
 CN Quinoline, 1,2,3,4-tetrahydro-1-[2-(4-phenyl-1-piperazinyl)ethyl]-,
 hydrochloride (6CI) (CA INDEX NAME)
 MF C21 H27 N3 . Cl H
 SR CAOLD
 LC STN Files: CAOLD
 CRN (110081-34-0)



● HCl

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L4 ANSWER 26 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 110081-34-0 REGISTRY
 CN Quinoline, 1,2,3,4-tetrahydro-1-[2-(4-phenyl-1-piperazinyl)ethyl]-
 (6CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C21 H27 N3
 CI COM
 SR CAOLD
 LC STN Files: BEILSTEIN*, CAOLD
 (*File contains numerically searchable property data)

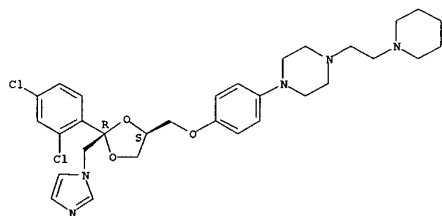


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

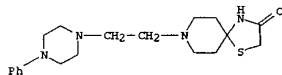
L4 ANSWER 27 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 75049-52-4 REGISTRY
 CN Piperazine,
 1-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-
 dioxolan-4-yl]methoxy]phenyl]-4-[2-(1-piperidinyl)ethyl]-, cis-
 (9CI) (CA INDEX NAME)
 FS STEREOSEARCH
 MF C31 H39 Cl2 N5 O3
 CI COM

Relative stereochemistry.



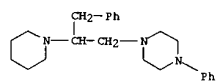
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 28 OF 29 REGISTRY COPYRIGHT 2002 ACS
 RN 54950-44-6 REGISTRY
 CN 1-Thia-4,8-diazaspiro[4.5]decan-3-one,
 8-[2-(4-phenyl-1-piperazinyl)ethyl]-
 (9CI) (CA INDEX NAME)
 FS 3D CONCORD
 MF C19 H28 N4 O S
 CI COM



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 29 OF 29 REGISTRY COPYRIGHT 2002 ACS
RN 7029-67-6 REGISTRY
CN Piperazine, 1-phenyl-4-(3-phenyl-2-piperidinopropyl)- (7CI, 8CI) (CA
INDEX NAME)
FS 3D CONCORD
MF C24 H33 N3
LC STN Files: BEILSTEIN*, CAOLD
(*File contains numerically searchable property data)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

```
=> fil caplus
COST IN U.S. DOLLARS                SINCE FILE      TOTAL
                                     ENTRY      SESSION
FULL ESTIMATED COST                190.48      190.69
```

FILE 'CAPLUS' ENTERED AT 13:22:49 ON 20 AUG 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8
FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> d his

(FILE 'HOME' ENTERED AT 13:21:47 ON 20 AUG 2002)

FILE 'REGISTRY' ENTERED AT 13:21:54 ON 20 AUG 2002

```
L1          STRUCTURE UPLOADED
L2          317 S L1 FUL
L3          288 S L2 AND CAPLUS/LC
L4          29 S L2 NOT L3
```

FILE 'CAPLUS' ENTERED AT 13:22:49 ON 20 AUG 2002

=> s l3

```
L5          211 L3
```

=>

Uploading 09764710.str

```
L6          STRUCTURE UPLOADED
```

=> s

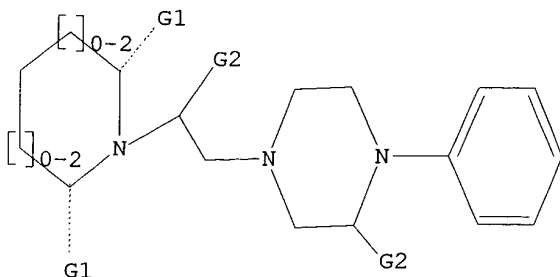
ENTER LOGIC EXPRESSION, QUERY NAME, OR (END):end

SEARCH ENDED BY USER

=> d

L6 HAS NO ANSWERS

L6 STR



G1 H, O, S

G2 H, Ak

Structure attributes must be viewed using STN Express query preparation.

=> fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

2.77

193.46

FILE 'REGISTRY' ENTERED AT 13:26:55 ON 20 AUG 2002

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STRUCTURE FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

DICTIONARY FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s l6 subset=l2 ful

FULL SUBSET SEARCH INITIATED 13:27:08 FILE 'REGISTRY'

FULL SUBSET SCREEN SEARCH COMPLETED - 317 TO ITERATE

100.0% PROCESSED 317 ITERATIONS
SEARCH TIME: 00.00.01

265 ANSWERS

L7 265 SEA SUB=L2 SSS FUL L6

=> s 17 not 12

L8 0 L7 NOT L2

=> s 17 and caplus/lc

23929408 CAPLUS/LC

L9 255 L7 AND CAPLUS/LC

=> fil caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

37.43

230.89

FILE 'CAPLUS' ENTERED AT 13:27:34 ON 20 AUG 2002

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FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8

FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s 19

L10 194 L9

=> fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.40

231.29

FILE 'REGISTRY' ENTERED AT 13:27:59 ON 20 AUG 2002

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STRUCTURE FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5
DICTIONARY FILE UPDATES: 19 AUG 2002 HIGHEST RN 444278-83-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s 17 ful
FULL SEARCH INITIATED 13:28:03 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 6498 TO ITERATE

100.0% PROCESSED 6498 ITERATIONS 481 ANSWERS
SEARCH TIME: 00.00.01

L11 481 SEA SSS FUL L6

=> s l11 and caplus/lc
23929408 CAPLUS/LC
L12 444 L11 AND CAPLUS/LC

| => fil caplus | SINCE FILE | TOTAL |
|----------------------|------------|---------|
| COST IN U.S. DOLLARS | ENTRY | SESSION |
| FULL ESTIMATED COST | 144.66 | 375.95 |

FILE 'CAPLUS' ENTERED AT 13:28:54 ON 20 AUG 2002
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FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8
FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l12
L13 263 L12

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 0.40 | 376.35 |

FILE 'CAPLUS' ENTERED AT 13:29:27 ON 20 AUG 2002
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FILE COVERS 1907 - 20 Aug 2002 VOL 137 ISS 8
FILE LAST UPDATED: 19 Aug 2002 (20020819/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

=> s l13
L14 263 L12

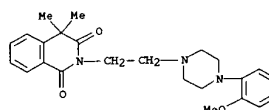
=> d 1-263 ibib abs hitstr

L14 ANSWER 1 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:521523 CAPLUS
DOCUMENT NUMBER: 137:73273
TITLE: Adrenergic receptor ligand-neurotoxin conjugates
and
methods for treating pain
INVENTOR(S): Gil, Daniel W.; Aoki, Kei Roger
PATENT ASSIGNEE(S): Allergan Sales, Inc., USA
SOURCE: PCT Int. Appl., 76 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2002053177 | A2 | 20020711 | WO 2001-US48651 | 20011214 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| FW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: US 2000-751053 A 20001229
OTHER SOURCE(S): MARPAT 137:73273
AB Agents for treating pain, methods for producing the agents, and methods
for treating pain by administration to a patient of a therapeutically effective amt. of the agent, are disclosed. The agent may include a clostridial neurotoxin, a fragment or a deriv. thereof, attached to a targeting component, wherein the targeting component is selected from a group consisting of compds. which selectively binds at the .alpha.2b or .alpha.2b/.alpha.2c adrenergic receptor subtype(s) as compared to other binding sites, e.g. the .alpha.2a adrenergic receptor subtype.
IT 67339-62-2B, ARC 239, conjugates
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adrenergic receptor ligand-neurotoxin conjugates and methods for treating pain)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 1 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

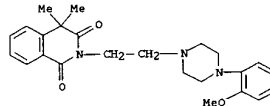


L14 ANSWER 2 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2002:408903 CAPLUS
DOCUMENT NUMBER: 136:395968
TITLE: Remedies for digestive functional disorder and screening method
INVENTOR(S): Yamamoto, Osamu
PATENT ASSIGNEE(S): Nippon Shinyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2002042765 | A1 | 20020530 | WO 2001-JP10152 | 20011121 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| FW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: JP 2000-356040 A 20001122
AB Medicinal compns. contg. as the active ingredient an adrenergic .alpha.2B receptor selective antagonist, an adrenergic .alpha.2C receptor selective antagonist or an adrenergic .alpha.2B/2C receptor selective antagonist;
and a method of screening the same. Namely, medicinal compns. for treating irritable bowel syndrome which have an excellent effect of improving enteric movement and a high safety; and a method useful in screening the same.
IT 67339-62-2, ARC239
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adrenergic .alpha.2 B and C antagonists as remedies for digestive functional disorder and screening method)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 2 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 3 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:392232 CAPLUS
 DOCUMENT NUMBER: 136:401912
 TITLE: Nitrosated and nitrosylated alpha-adrenergic receptor
 INVENTOR(S): antagonist compounds, compositions and their uses
 Garvey, David S.; Schroeder, Joseph D.; Saenz de Tejada, Inigo
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 40 pp., Cont.-in-part of U.S.
 Ser. No. 714,313.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 7
 PATENT INFORMATION:

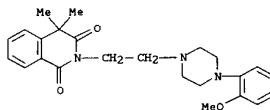
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2002061879 | A1 | 20020523 | US 2001-24550 | 20011221 |
| US 5932538 | A | 19990803 | US 1996-595732 | 19960202 |
| US 5994294 | A | 19991130 | US 1996-714313 | 19960918 |
| PRIORITY APPLN. INFO.: | | | US 1996-595732 | A2 19960202 |
| | | | US 1996-714313 | A2 19960918 |

OTHER SOURCE(S): MARPAT 136:401912
 GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention is directed to nitrosated or nitrosylated a-adrenergic receptor antagonists, e.g. I [Ra = H, alkoxy; Rb = NMe(CH₂)nHCO₂R, 6,7-dimethoxy-1,2,3,4-tetrahydroisoquinolin-2-yl; a = 2, 3; Rc = heteroaryl, heterocycle, lower alkyl, hydroxyalkyl, arylheterocycle; D = NO, NO₂, C(Rd)OC(O)YZ(CReRf)PTQ; Rd = H, lower alkyl, cycloalkyl, aryl alkyl, heteroaryl; Y = O, S, C, NRi; Ri = H, lower alkyl; Re, Rf = H, lower alkyl, haloalkyl, cycloalkyl, alkoxy, aryl, heteroaryl, NH₂, (di)alkylamino, amido, CO₂H, ester, TQ; ReRf = carbonyl, heterocycle, cycloalkyl; p = 1 - 10; T = bond, O, S, N; Z = bond, lower alkyl, haloalkyl, cycloalkyl, aryl, (CReRf)p, Q = NO, NO₂], II [R = CH₂N(C₆H₄Me-4)C₆H₄OB1-3, CH₂Ph, 2-methoxy-1,4-benzodioxin-2-yl, 1-methyl-2,3-dihydroisindol-2-yl, 5-chloro-2,3-dihydroisindol-2-yl; D1 = H, D], III [Rh = H, C(O)ORD, C(O)X; X = Y(CReRf)pG(CReRf)PTQ; G = bond, TC(O), C(O)T, C(YC(O)Rm); Rm = heteroaryl, heterocycle], IV [A1 = O, CH₂], V, (RmRkC)N(D1)(CRkRl) [Rk = H, lower alkyl; Rl = CH₂C₆H₄O(CH₂)hMe, CH₂C₆H₄OD, CH₂OC₆H₃(OMe)2-2,6, CH₂CH₂Ph; b = 0, 1; Rn = CH₂C₆H₄(SO₂NH₂)-3,

L14 ANSWER 3 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 1-oxotetralin-2-yl, 1,4-benzodioxin-2-yl] and RpRkCHCH(Ro)OD [Ro = (1-naphthyl)oxy)methyl, C₆H₄OB1; Rp = 4-benzylpiperidino, 4-(2-methoxyphenyl)piperazino]. The present invention is also directed to compns. comprising .alpha.-adrenergic receptor antagonists that are optionally substituted with at least one NO or NO₂ moiety and compds. that donate, transfer or release nitric oxide or elevate levels of endogenous endothelium-derived relaxing factor, and methods for treating sexual dysfunctions in males and females. Thus, S-Nitroso-glutathione was prepd. from glutathione via reaction with NaNO₂ in aq. HCl. S-Nitroso-glutathione at 500 .mu.g was able to induce near maximal erectile response in anesthetized rabbits.
 IT 67339-62-2D, ARC 239, nitrosated or nitrosylated RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (prepn. of nitrosated and nitrosylated alpha-adrenergic receptor antagonist compds., compns. and their uses)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



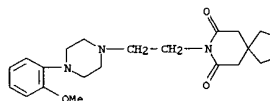
L14 ANSWER 4 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:368310 CAPLUS
 DOCUMENT NUMBER: 136:368366
 TITLE: Serotonergic compositions and methods for treatment of mild cognitive impairment
 INVENTOR(S): Wurtman, Richard J.; Lee, Robert K. K.
 PATENT ASSIGNEE(S): Massachusetts Institute of Technology, USA
 SOURCE: PCT Int. Appl., 34 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2002038142 | A2 | 20020516 | WO 2001-US43016 | 20011108 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, EG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, EE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 PRIORITY APPLN. INFO.:

AB A method of treating mild cognitive impairment is disclosed. The method comprises administering an effective amt. of a serotonergic agent, including, but not limited to, dexnorfenfluramine. The agent can be any serotonergic agonist, partial agonist, serotonin reuptake inhibitor, or combinations of these agents. The treatment method also encompasses combinations of serotonergic agents and nonsteroidal antiinflammatory agents. The treatment method may also delay the onset of mild cognitive impairment, dementia, or both.
 IT 21102-95-4, EMY 7378
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (serotonergic compns. and methods for treatment of mild cognitive impairment)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

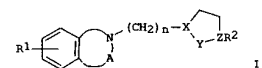
L14 ANSWER 4 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● 2 HCl

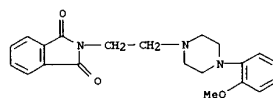
L14 ANSWER 5 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:314042 CAPLUS
 DOCUMENT NUMBER: 137:78925
 TITLE: Design, synthesis and biological activity study
 on
 N-[4-(substituted phenyl)piperazine-1-yl]alkyl
 amide
 series as .alpha.1-adrenoceptor antagonists
 AUTHOR(S): Fang, Hao; Xia, Lin; Jiang, Zhen-Zhou; Zhang,
 Wei;
 CORPORATE SOURCE: Zhang, Lu-Yong
 Department of Medicinal Chemistry, China
 Pharmaceutical University, Nanjing, 210009,
 Peop. Rep.
 SOURCE: Huaxue Xuebao (2002), 60(4), 725-731
 CODEN: HXHPA4; ISSN: 0567-7351
 PUBLISHER: Kekue Chubanshe
 DOCUMENT TYPE: Journal
 LANGUAGE: Chinese
 OTHER SOURCE(S): CASREACT 137:78925
 AB Novel furan-2-carboxylic acid (.omega.-[4-(substituted
 phenyl)piperazine-1-yl]alkyl)amide and
 2-oxo-2H-chromene-3-carboxylic
 acid (.omega.-[4-(substituted phenyl)piperazine-1-yl]alkyl)amide
 derives.
 have been designed and synthesized based on the structure and
 activity
 relationship (SAR) of phenylpiperazine series as
 .alpha.1-adrenoceptor
 (.alpha.1-AR) antagonists and the results of computer-aided drug
 design we
 studied before. All the target compds. have been identified by 1H
 NMR, 1H
 and MS (HRMS). Preliminary bioassay suggests that most of the target
 compds. display good blocking activity to .alpha.1-AR. The potency
 (pA2)
 of compd. N-[2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl]-2-
 furancarboxamide is higher than prazosin.
 IT 99718-67-9P 117046-73-8P 440117-82-8P
 440117-88-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT
 (Reactant or reagent)
 (synthesis and biol. activity of phenylpiperazinylalkyl amides as
 .alpha.1-adrenoceptor antagonists)
 RN 99718-67-9 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione,
 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-
 (9CI) (CA INDEX NAME)

L14 ANSWER 6 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:31419 CAPLUS
 DOCUMENT NUMBER: 136:85830
 TITLE: Preparation of bicyclic lactams and sulfonamides
 as
 5-HT1A agonists
 INVENTOR(S): Steiner, Gerd; Schellhaas, Kurt; Szabo, Laszlo;
 Behl,
 Berthold; Garcia-Ladona, Francisco Javier; Unger,
 Lilliane
 PATENT ASSIGNEE(S): Knoll GmbH, Germany
 SOURCE: PCT Int. Appl., 39 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:
 PATENT NO. KIND DATE APPLICATION NO. DATE
 WO 2002002529 A1 20020110 WO 2001-EP7571 20010702
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH,
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 CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE,
 GH,
 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
 LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL,
 PT,
 RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
 US,
 UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 KW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH,
 CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 DE 10031391 A1 20020207 DE 2000-10031391 20000703
 PRIORITY APPLN. INFO.: DE 2000-10031391 A 20000703
 OTHER SOURCE(S): MARPAT 136:85830
 GI

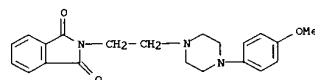


AB Title compds. [I; the ring including NA can be a 5-7 membered ring
 contg.
 O, S, or double bond; A = CO, SO2; X = N; Y = CH2, CH2CH2, (CH2)3,
 CH2CH2
 Z = N, C, CH; n = 2-4; R1 = H, halo, alkyl, CF3, OH, alkoxy, amino;
 R2 =

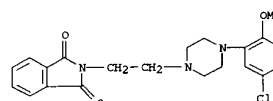
L14 ANSWER 5 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



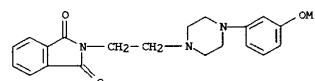
RN 117046-73-8 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione,
 2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-
 (9CI) (CA INDEX NAME)



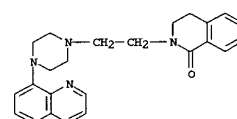
RN 440117-82-8 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-[4-(5-chloro-2-methoxyphenyl)-1-
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 440117-88-4 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione,
 2-[2-[4-(3-methoxyphenyl)-1-piperazinyl]ethyl]-
 (9CI) (CA INDEX NAME)



L14 ANSWER 6 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 (substituted) (anellated) Ph, pyridyl, pyrazinyl and salts thereof,
 were
 prepd. Thus, isoquinoline in DMF was stirred with NaH for 30 min.
 followed by addn. of 1-[4-(2-chloroethyl)-1-piperazinyl]isoquinoline
 (prepn. given) and stirring for 2 h at 80.degree. to give 82%
 2-[2-(4-(1-isoquinolinyl)-1-piperazinyl)ethyl]-1(2H)-
 isoquinoline.2HCl.2H2O. Tested 1 showed affinity for the 5-HT1A
 receptor
 with Ki = 0.1-5.4 nM in HEK 293 cells.
 IT 387399-38-4P
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
 (Uses)
 (prepn. of bicyclic lactams and sulfonamides as 5-HT1A agonists)
 RN 387399-38-4 CAPLUS
 CN 1(2H)-Isoquinolinone, 3,4-dihydro-2-[2-[4-(8-quinolinyl)-1-
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

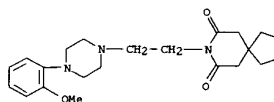


REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 7 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:2436 CAPLUS
 DOCUMENT NUMBER: 136:226674
 TITLE: A-315456: a selective .alpha.1D-adrenoceptor antagonist with minimal dopamine D2 and 5-HT1A receptor affinity
 AUTHOR(S): Buckner, Steven A.; Milicic, Ivan; Daza, Anthony; Lynch, James J.; Kolasa, Teodzyj; Nakane, Masaki;
 CORPORATE SOURCE: Sullivan, James P.; Brioni, Jorge D. Abbott Laboratories, Abbott Park, IL, 60064-6118, USA
 SOURCE: European Journal of Pharmacology (2001), 433(1), 123-127
 CODEN: EJPHAZ; ISSN: 0014-2999
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In functional assays, A-315456, N-[3-(cyclohexylidene-(1H-imidazol-4-ylmethyl))phenyl]ethanesulfonamide, behaved as an .alpha.1D-adrenoceptor subtype selective antagonist (pA2=8.34) in the rat aorta. It was 93-fold less potent at the .alpha.1B-adrenoceptor subtype expressed in the rat spleen, and was inactive at the .alpha.1A-adrenoceptor subtype expressed in the rat vas deferens. Radioligand binding assays also revealed high affinity (pKi=8.71) for the .alpha.1D-adrenoceptor subtype and weaker affinities at the .alpha.1A-adrenoceptor (pKi=6.23) and .alpha.1B-adrenoceptor (pKi=7.86). In comparison to its potent affinity at the .alpha.1D-adrenoceptor subtype, A-315456 was 3020-, 794- and 38-fold weaker at the dopamine D2-, 5-HT1A-, and .alpha.2A-adrenoceptors, resp. These studies indicate that A-315456 is a potent and selective .alpha.1D-antagonist that may serve as a useful pharmacol. ligand to probe the physiol. role of the .alpha.1D-adrenoceptor subtype in normal and disease states.
 IT 21102-95-4, RMY-7378 255893-38-0, SNAP 8719
 RL: PAC (Pharmacological activity); BIOL (Biological study) (A-315456, a selective .alpha.1D-adrenoceptor antagonist with minimal dopamine D2 and 5-HT1A receptor affinity)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 8 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:789964 CAPLUS
 DOCUMENT NUMBER: 136:64512
 TITLE: Functional characterization of .alpha.1-adrenoceptor subtypes in human subcutaneous resistance arteries
 AUTHOR(S): Jarajapu, Yagna P. R.; Johnston, Fiona; Berry, Colin;
 Renwick, Andrew; McGrath, John C.; MacDonald, Allan;
 CORPORATE SOURCE: Millier, Chris Vascular Assessment Unit, School of Biological and Biomedical Sciences, Glasgow Caledonian University,
 SOURCE: Glasgow, UK
 Therapeutics Journal of Pharmacology and Experimental (2001), 299(2), 729-734
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The functional characteristics of the .alpha.1-adrenoceptor subtypes in human resistance arteries are still not clear. The authors recently reported that the .alpha.1A-adrenoceptor predominantly mediates contraction to norepinephrine in human skeletal muscle resistance arteries. In this study the authors extended these investigations to human s.c. resistance arteries. Arterial segments were isolated from the inguinal s.c. fat and mounted on a small vessel wire myograph. Potencies of agonists and antagonists were examd.
 N-[5-(4,5-dihydro-1H-imidazol-2-yl)-2-hydroxy-5,6,7,8-tetrahydronaphthalen-1-yl]methanesulfonamide (A-61603) was found to be 10- and 54-fold more potent than norepinephrine and phenylephrine, resp. Brimonidine (UK 14304) evoked significantly smaller contractile responses than norepinephrine and phenylephrine, showing the presence of a small population of .alpha.2-adrenoceptors in these arteries, and this was confirmed by the studies with selective .alpha.1- and .alpha.2-adrenoceptor antagonists prazosin and (8aR, 12aS, 13aS)-5,8,8a,9,10,11,12,12a,13a-decahydro-3-methoxyl-12-(ethylsulfonyl)-6H-isoquino[2,1-g][1,6]-naphthyridine (RS 79948). Prazosin, 5-methyl-urapidil, and 2-[2,6-dimethoxyphenoxylethyl]aminomethyl-1,4-benzodioxane (WB 4101) shifted the potency of norepinephrine concn. dependently giving pA2 values of 9.4, 8.9, and 10.1, resp., showing the presence of the .alpha.1A-subtype in these arteries. Pretreatment with 1

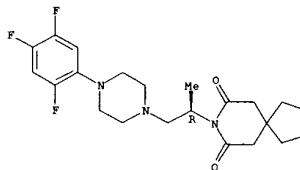
L14 ANSWER 7 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●2 HCl

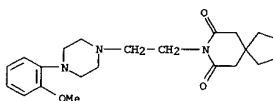
RN 255893-38-0 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 8 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 and 10 .mu.M chloroethylclonidine did not affect the potency of and max. responses to norepinephrine, ruling out the presence of the .alpha.1B-subtype in these arteries. 8-[2-[4-(2-Methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4.5]decane-7,9-dione (RMY 7378, 10 and 100 nM) did not affect the potency of norepinephrine but a small shift was obsd. by 1 .mu.M RMY 7378, giving a pKB value of 7.1, much less than that reported for the .alpha.1D-subtype. These results suggest the predominant involvement of .alpha.1A-adrenoceptor in the contractile responses to norepinephrine in these arteries. The physiol. role of this subtype in the maintenance of peripheral arterial resistance is yet to be confirmed.
 IT 21102-95-4, RMY 7378
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (pharmacol. characterization of .alpha.1-adrenoceptor subtypes in human s.c. resistance arteries)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 9 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:781185 CAPLUS
DOCUMENT NUMBER: 135:328176
TITLE: Polymorphisms in human .alpha.2 adrenergic receptor
INVENTOR(S): genes and their diagnostic and therapeutic uses
Liggett, Stephen B.; Small, Kirsten M.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 163 pp.
CODEN: PIXKD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2001079561 | A2 | 20011025 | WO 2001-US12575 | 20010417 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, VZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |

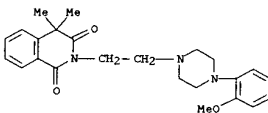
PRIORITY APPLN. INFO.:
US 2000-551744 A 20000417
US 2000-636259 A 20000810
US 2000-692077 A 20001019

AB The present invention includes polymorphisms in nucleic acids encoding the .alpha.2B, .alpha.2A, and .alpha.2C adrenergic receptor genes and expressed .alpha.2B, .alpha.2A and .alpha.2C adrenergic receptor protein mol. The invention also pertains to methods and mols. for detecting such polymorphisms. The invention further pertains to the use of such mols. and methods in the diagnosis and treatment of diseases such as cardiovascular and central nervous system disease. Genetic polymorphisms of deletion/insertions and single nucleotides in the intracellular loop 3 region of human .alpha.2 adrenergic receptors were identified and characterized to search for correlations between the polymorphisms and physiol. signaling functions of the receptors. Recombinant polymorphic receptor proteins were expressed in cell lines to measure ligand binding,

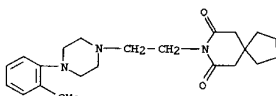
L14 ANSWER 10 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:776249 CAPLUS
DOCUMENT NUMBER: 137:433
TITLE: The hypotensive effect of RMY 7378 is antagonized by a silent 5-HT1A receptor antagonist: Comparison with 8-hydroxy-dipropylamino tetralin
AUTHOR(S): Villalobos-Molina, Rafael; Lopez-Guerrero, J. Javier;
CORPORATE SOURCE: Ibarra, Maximiliano
Departamento de Farmacobiologia, Centro de Investigacion y de Estudios Avanzados (CINVESTAV), Instituto Politecnico Nacional (IPN), Mexico City, 14000, Mex.
SOURCE: Archives of Medical Research (2001), 32(5), 389-393
CODEN: ABDEER; ISSN: 0188-4409
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Stimulation of central 5-HT1A receptors produces bradycardia and diminishes blood pressure in conscious or anesthetized rats. Our objective was to investigate the effects on blood pressure and heart rate of the partial 5-HT1A receptor agonist and selective .alpha.1D-adrenoceptor antagonist RMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro [4.5] decane-7,9 dione hydrochloride) compared to the full 5-HT1A receptor agonist 8-OH-DPAT (8-hydroxy-dipropylamino tetralin) in adult anesthetized rats. Male Wistar rats of 6 mo of age were exposed i.v. (i.v.) to increasing doses of RMY 7378 or 8-OH-DPAT in the absence and presence of WAY 100635. Blood pressure and heart rate were continuously recorded. RMY 7378 induced a decrease in blood pressure with no apparent change in heart rate compared to basal values, while 8-OH-DPAT decreased both hemodynamic parameters. RMY 7378 hypotensive effect was antagonized by the selective, silent 5-HT1A receptor antagonist WAY 100635 (N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N-(2-pyridinyl) cyclohexanecarboxamide trihydrochloride). However, a remnant yet significant hypotensive effect was not blocked by the antagonist. In contrast, 8-OH-DPAT actions were completely blocked by WAY 100635. Data suggest that RMY 7378 cardiovascular effects are related to activation, as a full agonist, of central 5-HT1A receptors in adult rats; however, participation of other systems such as vascular .alpha.1-adrenoceptors in

L14 ANSWER 9 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
protein phosphorylation, effect on adenylyl cyclase activity, MAP kinase activation, GTP.gamma.S binding, and/or inositol phosphate accumulation. Differences in signal transduction due to the .alpha.2 adrenoceptor polymorphisms were obsd. but the polymorphisms have not yet been genetically linked with disease, for example hypertension. The polymorphisms of this invention can be used to det. an individual's risk for developing a disease, for diagnosis, and for selecting appropriate drug treatments based on the identity of the polymorphism.
IT 67339-62-2, ARC 239
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (polymorphisms in human .alpha.2 adrenergic receptor genes and their diagnostic and therapeutic uses)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 10 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
cardiovascular function is suggested.
IT 21102-95-4, RMY 7378
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); BIOL (Biological study)
(hypotensive effect of RMY 7378 is antagonized by a silent 5-HT1A receptor antagonist: comparison with 8-OH-DPAT)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



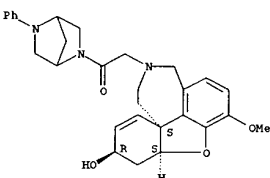
● 2 HCl

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RECORD.
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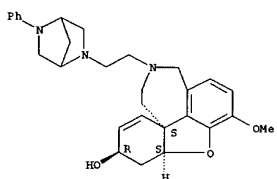
L14 ANSWER 11 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:747793 CAPLUS
DOCUMENT NUMBER: 135:304054
TITLE: Preparation of galanthamine analogs for pharmaceutical use as acetyl- and butyrylcholinesterase inhibitors
INVENTOR(S): Jordis, Ulrich; Froehlich, Johannes; Treu, Matthias;
Beate; Hirschschall, Manfred; Czollner, Laszlo; Kaelz, Welzig, Stefan
PATENT ASSIGNEE(S): Sanochemia Pharmazeutika Aktiengesellschaft, Austria
SOURCE: PCT Int. Appl., 285 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-------------------|------------|
| WO 2001074820 | A1 | 20011011 | WO 2001-AT82 | 20010322 |
| W: AE, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, CA, CH, CN, CU, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, A2, BY, KG, KZ, MD, RU, T.J. TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, EJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1181294 | A1 | 20020227 | EP 2001-914813 | 20010322 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, IE, SI, LT, LV, FI, RO | | | | |
| BR 2001005563 | A | 20020402 | BR 2001-5563 | 20010322 |
| NO 2001005857 | A | 20020129 | NO 2001-5857 | 20011130 |
| PRIORITY APPLN. INFO.: | | | AT 2000-546 | A 20000331 |
| | | | AT 2001-238 | A 20010215 |
| | | | WO 2001-AT82 | W 20010322 |
| OTHER SOURCE(S): | | | MARPAT 135:304054 | |
| G1 | | | | |

L14 ANSWER 11 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

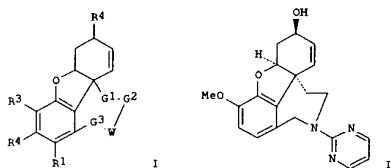


IT 365570-78-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of galanthamine analogs for pharmaceutical use as acetyl- and butyrylcholinesterase inhibitors)
RN 365570-78-1 CAPLUS
CN 6H-Benzofuro[3a,3,2-ef][2]benzazepin-6-ol, 4a,5,9,10,11,12-hexahydro-3-methoxy-11-[2-(5-phenyl-2,5-diazabicyclo[2.2.1]hept-2-yl)ethyl]-, (4aS,6R,8aS)-(9CI) (CA INDEX NAME)
Absolute stereochemistry.



REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

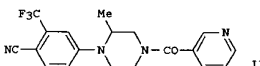
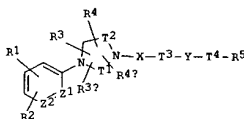
L14 ANSWER 11 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB Galanthamine derivs. and analogs, such as I [R1, R2 = H, Cn, OH, SH, NO2, SO3H, PO3H, NH2, halogen, etc.; R3 = OH, OMe; R4 = OH, alkyloxy, alkenyloxy, alkynyloxy, cycloalkyloxy, aryl, etc.; G1, G2, G3 = CH2, (CH2)2, (CH2)3, CH(OH), etc.; W = CH2, NR5, etc.; R5 = alkyl, acyl, aryl, etc.], were prepd. for therapeutic use as acetyl- and butyrylcholinesterase inhibitors. Thus, (+-)-galanthamine deriv. II was prepd. in 80.8% yield by condensation of (+-)-norgalanthamine with 2-chloropyrimidine using NaHCO3 in EtOH. The prepd. galanthamine derivs. and analogs were tested for acetyl- and butyrylcholinesterase inhibiting activity.
IT 365570-78-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses) (prepn. of galanthamine analogs for pharmaceutical use as acetyl- and butyrylcholinesterase inhibitors)
RN 365570-78-9 CAPLUS
CN 2,5-Diazabicyclo[2.2.1]heptane, 2-phenyl-5-[[4aS,6R,8aS]-4a,5,9,10-tetrahydro-6-hydroxy-3-methoxy-6H-benzofuro[3a,3,2-ef][2]benzazepin-11(12H)-yl]acetyl]- (9CI) (CA INDEX NAME)
Absolute stereochemistry.

L14 ANSWER 12 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:704727 CAPLUS
DOCUMENT NUMBER: 135:257268
TITLE: Preparation of piperazinylbenzonitrile analogs as antiandrogen agents
INVENTOR(S): Taniguchi, Nobuaki; Inamura, Masakazu; Kinoyama, Isao; Samizu, Kiyohiro; Kawanami, Eiji; Okada, Minoru; Kotoku, Hiroshi
PATENT ASSIGNEE(S): Yamanouchi Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 27 pp.
CODEN: JKKXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

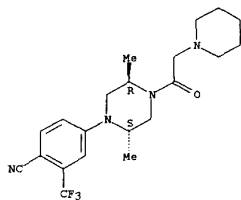
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------|------|----------|-------------------|----------|
| JP 2001261657 | A2 | 20010926 | JP 2000-74999 | 20000317 |
| OTHER SOURCE(S): | | | MARPAT 135:257268 | |
| G1 | | | | |



AB The title compds. I [R1, R2 = H, halo, etc.; R3, R3a, R4, R4a = H, alkyl, etc.; T1 = (CH2)m; T2 = (CH2)n; T3 = (Alk1)p; T4 = (Alk2)q; R5 = (un)substituted carbamoyl, etc.; Alk1, Alk2 = (un)substituted alkylene, etc.; m, n = 1 - 3; p, q = 0 or 1; Z1, Z2 = CH, N; Y = bond, O, etc.; X = CO, etc.], useful as antiandrogen agents (no data), are prepd. For example, the title compd. II was prepd.
IT 362471-49-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological

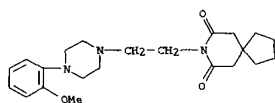
L14 ANSWER 12 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
 use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of piperazinylbenzoxazole derivs. and analogs as
 antiandrogen
 agents)
 RN 362471-49-6 CAPLUS
 CN Piperazine, 1-[4-cyano-3-(trifluoromethyl)phenyl]-2,5-dimethyl-4-(1-
 piperidinylacetyl)-, (2S,5R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L14 ANSWER 13 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:626800 CAPLUS
 DOCUMENT NUMBER: 135:366874
 TITLE: Molecular cloning and functional expression of the
 guinea pig .alpha.1A-adrenoceptor
 Gonzalez-Espinosa, C.; Romero-Avila, M. T.;
 Mora-Rodriguez, D. M.; Gonzalez-Espinosa, D.;
 Garcia-Sainz, J. A.
 CORPORATE SOURCE: Departamento de Biologia Celular, Universidad
 Nacional
 Autonoma de Mexico, Instituto de Fisiologia
 Celular,
 Mexico City, 04510, Mex.
 SOURCE: European Journal of Pharmacology (2001), 426(3),
 147-155
 CODEN: EJPHAL; ISSN: 0014-2999
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In the present paper, the cloning and expression of the guinea pig
 .alpha.1A-adrenoceptor is presented. The nucleotide sequence had an
 open
 reading frame of 1401 bp that encoded a 466 amino-acid protein with an
 estd. mol. mass of .apprxq.51.5 kDa. When the clone was expressed in
 Cos-1 cells, specific high-affinity binding of [3H]prazosin and
 [3H]tamsulosin was obsd. Chloroethylclonidine treatment of membranes
 slightly decreased the total binding with both radioligands. Binding
 competition expts. using [3H]tamsulosin showed the following potency
 order: (a) for agonists:
 oxymetazoline.mchgt.epinephrine>norepinephrine>me
 thoxamine, and (b) for antagonists: prazosin.gtoreq.5-methyl-
 urapidil>benoxathian>phenolamine.mchgt.BMY 7378 (8-[2-[4-(2-
 methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4,5]decane-7,9-dione).
 Photoaffinity labeling using [125I-aryl]azido-prazosin revealed a
 major
 broad band with a mol. mass between 70 and 80 kDa. The receptor was
 functional, as evidenced by an epinephrine-increased prodn. of
 [3H]inositol phosphates that was blocked by prazosin.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BPR
 (Biological
 process); BSU (Biological study, unclassified); BIOL (Biological
 study);
 PROC (Process)
 (mol. cloning, functional expression and pharmacoI.
 characterization of
 guinea pig .alpha.1A-adrenoceptor)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 13 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

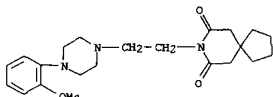


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REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 14 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:522422 CAPLUS
 DOCUMENT NUMBER: 135:327647
 TITLE: Phe-308 and Phe-312 in transmembrane domain 7 are
 major sites of .alpha.1-adrenergic receptor
 antagonist
 binding: imidazoline agonists bind like
 antagonists
 AUTHOR(S): Waugh, David J. J.; Gaivin, Robert J.; Zuscik,
 Michael
 J.; Gonzalez-Cabrera, Pedro; Ross, Sean A.; Yun,
 June;
 Perez, Dianne M.
 CORPORATE SOURCE: Department of Molecular Cardiology NBS, The Lerner
 Research Institute, The Cleveland Clinic
 Foundation,
 Cleveland, OH, 44195, USA
 SOURCE: Journal of Biological Chemistry (2001), 276(27),
 25366-25371
 CODEN: JBCHA3; ISSN: 0021-9258
 PUBLISHER: American Society for Biochemistry and Molecular
 Biology
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Although agonist binding in adrenergic receptors is fairly well
 understood
 and involves residues located in transmembrane domains 3 through 6,
 there
 are few residues reported that are involved in antagonist binding. In
 fact, a major docking site for antagonists has never been reported in
 any
 G-protein coupled receptor. It has been speculated that antagonist
 binding is quite diverse depending upon the chem. structure of the
 antagonist, which can be quite different from agonists. We now
 report the
 identification of two phenylalanine residues in transmembrane domain
 7 of
 the .alpha.1A-adrenergic receptor (Phe-312 and Phe-308) that are a
 major
 site of antagonist affinity. Mutation of either Phe-308 or Phe-312
 resulted in significant losses of affinity (4-1200-fold) for the
 antagonists prazosin, WB4101, BMY7378, (+) niquindine, and
 5-methylurapidil, with no changes in affinity for phenethylamine-type
 agonists such as epinephrine, methoxamine, or phenylephrine.
 Interestingly, both residues are involved in the binding of all
 imidazoline-type agonists such as oxymetazoline, cirazoline, and
 clonidine, confirming previous evidence that this class of ligand
 binds
 differently than phenethylamine-type agonists and may be more
 antagonist-like, which may explain their partial agonist properties.
 In
 modeling these interactions with previous mutagenesis studies and
 using
 the current backbone structure of rhodopsin, we conclude that
 antagonist
 binding is docked higher in the pocket closer to the extracellular
 surface

L14 ANSWER 14 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
than agonist binding and appears skewed toward transmembrane domain
7.
IT 21102-95-4, BM7378
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
(Uses)
(Phe-309 and Phe-312 in transmembrane domain 7 are major sites of
.alpha.l-adrenergic receptor antagonist binding; imidazoline
agonists
bind like antagonists)
RN 21102-95-4 CAPLUS
CN 8-Azapiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



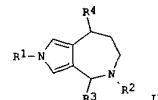
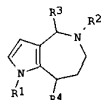
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REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:502429 CAPLUS
DOCUMENT NUMBER: 135:92553
TITLE: Synthesis and activity of pyrroloazepine
derivatives
as 5-HT antagonists
INVENTOR(S): Mizuno, Akira; Shibata, Makoto; Iwamori, Tomoe;
Shimamoto, Tetsuo; Nakanishi, Kyoko; Inomata,
Norio
PATENT ASSIGNEE(S): Suntory Ltd., Japan
U.S., 54 pp., Cont.-in-part of U.S. Ser. No.
875,455.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

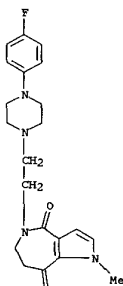
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|---|----------|-----------------|-------------|
| US 6258805 | B1 | 20010710 | US 1999-312713 | 19990517 |
| WO 9720845 | A1 | 19970612 | WO 1996-JP3522 | 19961202 |
| W: | AU, CA, HU, IL, JP, KR, US | | | |
| RW: | AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, | | | |
| PT, SE | | | | |
| US 5962448 | A | 19991005 | US 1997-875495 | 19970821 |
| US 2002072515 | A1 | 20020613 | US 2001-801816 | 20010309 |
| PRIORITY APPLN. INFO.: | | | JP 1995-335714 | A 19951201 |
| | | | JP 1996-46928 | A 19960209 |
| | | | WO 1996-JP3522 | W 19961202 |
| | | | US 1997-875495 | A2 19970821 |
| | | | US 1999-312713 | A1 19990517 |

OTHER SOURCE(S): MARPAT 135:92553
GI



AB Synthesis of pyrroloazepine derivs. (I) and (II) [R1 = H, alkyl, Ph, benzyl; R2 = substituted alkyl; R3, R4 independently = -O, -NOH, OH, OMe, SCH2CH2S] or pharmaceutically acceptable salts for use as 5-HT antagonists
is disclosed. Thus, I (R1 = Me, R2 = (CH2)2-piperazinyl-CGH4F, R3 = -O, R4 = OH) (III) was prepd. by condensation of 3-pyrrolocarboxylic acid with .beta.-alanine Et ester hydrochloride, the amide ester saponid. and the

L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
acid cyclized to pyrroloazepine with polyphosphoric acid, the
azepine N
alkylated with bromoalkylchloride followed by
1-(4-fluorophenyl)piperazine
and reduct. of carbonyl with NaBH4. III shows a 90.2% contraction at
10-7M
in 5-HT action assay. I and II have strong serotonin-2 receptor
antagonistic action and low toxicity and less side effects, and are
therapeutically useful in the treatment of circulatory diseases
and/or
conditions related thereto.
IT 191591-85-2P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); RCT (Reactant); SPN (Synthetic preparation);
THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT
(Reactant or reagent); USES (Uses)
(synthesis and activity of pyrroloazepine derivs. as 5-HT
antagonists)
RN 191591-85-2 CAPLUS
CN Pyrrolo[3,2-c]azepine-4,8(1H,5H)-dione, 5-[2-[4-(4-fluorophenyl)-1-
piperazinyl]ethyl]-6,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



PAGE 1-A

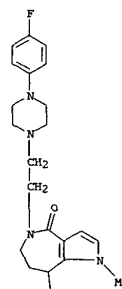
L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 2-A



IT 191592-08-2P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and activity of pyrroloazepine derivs. as 5-HT
antagonists)
RN 191592-08-2 CAPLUS
CN Pyrrolo[3,2-c]azepin-4(1H)-one, 5-[2-[4-(4-fluorophenyl)-1-
piperazinyl]ethyl]-6,6,7,8-tetrahydro-8-hydroxy-1-methyl- (9CI) (CA
INDEX
NAME)

PAGE 1-A



PAGE 2-A

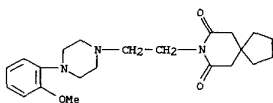


REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR
THIS

L14 ANSWER 15 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 16 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:473200 CAPLUS
DOCUMENT NUMBER: 135:283079
TITLE: Affinity of serotonin receptor antagonists and
agonists to recombinant and native
.alpha.1-adrenoceptor subtypes
AUTHOR(S): Yoshio, Rika; Taniguchi, Takanobu; Itoh, Harumi;
Muranatsu, Ikunobu
CORPORATE SOURCE: Departments of Pharmacology and Radiology, School
of
Medicine, Fukui Medical University, Fukui,
910-1193,
Japan
SOURCE: Japanese Journal of Pharmacology (2001), 86(2),
189-195
CODEN: JJPAAZ; ISSN: 0021-5198
PUBLISHER: Japanese Pharmacological Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Binding affinities of serotonin (5-HT)-receptor antagonists and
agonists
at human recombinant .alpha.1-adrenoceptor subtypes (.alpha.1a-
.alpha.1b- and .alpha.1d-subtypes) were examd. and compared with the
functional affinities obtained in rat caudal artery
(.alpha.1a-subtype),
dog carotid artery (.alpha.1b-subtype) and rat thoracic aorta
(.alpha.1d-subtype). Most of the 5-HT-receptor antagonists and
agonists
tested showed relatively high affinity to the three
.alpha.1-adrenoceptor
subtypes. The highest affinity (close to 1 nM) was found for NAN-190
(5-HT1A antagonist) in both binding and functional studies.
5-Methylurapidil (5-HT1A agonist) and BM7378 (5-HT1A agonist) showed,
resp., .alpha.1a(.alpha.1a)- and .alpha.1d(.alpha.1b)-subtype
selectivity
in both binding and functional affinities, but spiperone (5-HT2A
antagonist) showed .alpha.1b-selectivity only in binding affinity.
The
functional affinity of ritanserin (5-HT2A antagonist) to the
.alpha.1b-subtype was approx. 500-fold lower than that to the
.alpha.1b-subtype. The results show that many 5-HT-receptor
antagonists
and agonists have high affinity for .alpha.1-adrenoceptors but suggest
that there is a difference between their functional affinities and
binding
affinities in some cases.
IT 21102-95-4, RMY 7378
RL: BPR (Biological process); BSU (Biological study, unclassified);
BIOL
(Biological study); PROC (Process)
(serotonin receptor antagonists and agonists affinity for
.alpha.1-adrenoceptor subtypes in artery)
RN 21102-95-4 CAPLUS
CN 8-Azaspino[4,5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 16 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

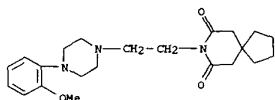


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REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 17 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:434868 CAPLUS
DOCUMENT NUMBER: 135:29141
TITLE: Use of .alpha.1 adrenergic receptor
subtype-selective
drugs in patients with acute myocardial infarction
INVENTOR(S): Schwinn, Debra A.
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 31 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
PATENT NO. KIND DATE APPLICATION NO. DATE

WO 2001041767 A1 20010614 WO 2000-US33135 20001207
W: AU, CA, JP
FW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,
NL,
PT, SE, TR
US 2001031460 A1 20011018 US 2000-731062 20001207
PRIORITY APPLN. INFO.: US 1999-169294P P 19991207
AB The invention discloses the use of .alpha.1a adrenergic
receptor-selective
and/or .alpha.1a/.alpha.1d-selective antagonists in a method of
preventing
restenosis after myocardial infarction and reperfusion. The invention
further discloses a method of identifying agents suitable for use in
such
a method.
IT 21102-95-4, RMY-7378
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES
(Uses)
(.alpha.1 adrenergic receptor subtype-selective drugs in patients
with
acute myocardial infarction, and vascular distribution of .alpha.1
adrenergic receptor subtypes)
RN 21102-95-4 CAPLUS
CN 8-Azaspino[4,5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

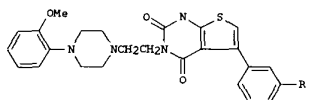


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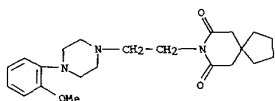
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 18 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:321149 CAPLUS
 DOCUMENT NUMBER: 135:137465
 TITLE: Two Novel and Potent 3-[(o-

Methoxyphenyl)piperazinyl-5-phenylthieno[2,3-d]pyrimidine-2,4-diones Selective for the .alpha.1D Receptor
 AUTHOR(S): Carroll, W. A.; Sippy, K. B.; Esbenshade, T. A.; Buckner, S. A.; Hancock, A. A.; Meyer, M. D.
 CORPORATE SOURCE: Neurological and Urological Diseases Research, Abbott Laboratories, Abbott Park, IL, 60064-6101, USA
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(9), 1119-1121
 CODEN: BMCLER; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



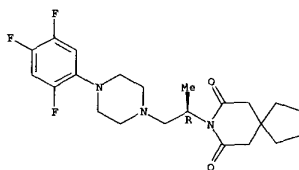
AB The synthesis and in vitro characterization of A-119637 (I, R = H) and A-123189 (I, R = Me), two novel, selective and potent .alpha.1D antagonists, are described.
 IT 21102-95-4, BMV7378 255893-38-0, SNAP 8719
 RL: RAC (Biological activity or effector, except adverse); RSU (Biological study, unclassified); BIOL (Biological study) (binding to .alpha.1D receptor)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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RN 255893-38-0 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

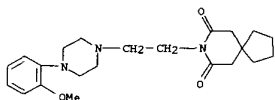


REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 19 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:207647 CAPLUS
 DOCUMENT NUMBER: 134:305637

TITLE: Failure of AH11110A to functionally discriminate between .alpha.1-adrenoceptor subtypes A, B and D or between .alpha.1- and .alpha.2-adrenoceptors
 AUTHOR(S): Eltze, M.; Knig, H.; Ullrich, B.; Grebe, T.
 CORPORATE SOURCE: Byk Gulden, Department of Pharmacology, Konstanz, D-78467, Germany
 SOURCE: European Journal of Pharmacology (2001), 415(2,3), 265-276
 CODEN: EJPHAZ; ISSN: 0014-2999
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The potency of the putatively .alpha.1B-adrenoceptor selective drug, 1-[biphenyl-2-yloxy]-4-imino-4-piperidin-1-yl-butan-2-ol (AH11110A), to antagonize contraction upon stimulation of .alpha.1A-adrenoceptors in rat vas deferens and rat perfused kidney, .alpha.1B-adrenoceptors in guinea-pig spleen, mouse spleen and rabbit aorta, and .alpha.1D-adrenoceptors in rat aorta and pulmonary artery was evaluated and compared to that of a no. of subtype-discriminating antagonists.
 N-[3-[4-(2-Methoxyphenyl)-1-piperazinyl]propyl]-3-methyl-4-oxo-2-phenyl-4H-1-benzopyran-8-carboxamide (Rac 15/2739) and (+-)-1,3,5-trimethyl-6-[[3-[4-((2,3-dihydro-2-hydroxymethyl)-1,4-benzodioxin-5-yl)-1-piperazinyl]propyl]amino]-2,4-(1H,3H)-pyrimidinedione (B8805-033) were confirmed as selective for .alpha.1A-adrenoceptors, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4.5]decane-7,9-dione (RMY 7378), 8-[2-[(1,4-benzodioxan-2-ylmethylamino)ethyl]-8-azaspiro[4.5]decane-7,9-dione (MDL 73005EF), and cystazosin were found to be selective for .alpha.1D-adrenoceptors, whereas spiperone was weakly selective for .alpha.1B-over .alpha.1A-adrenoceptors. However, from the functional affinity profile obtained for AH11110A at .alpha.1A-adrenoceptors (pA2=6.41 in rat vas deferens), .alpha.1B-adrenoceptors (pA2=5.49-6.54) and .alpha.1D-adrenoceptors (pA2=5.47-5.48), the affinity and presumed selectivity previously obtained for AH11110A in radioligand binding studies at native .alpha.1B- and cloned .alpha.1B-adrenoceptors (pKi=7.10-7.73) could not be confirmed. Addnl., AH11110A enhanced the general contractility of rat vas deferens, produced a bell-shaped dose-response curve of vasodilation in perfused rat kidney, and its antagonism in most other tissues was not simply competitive. The affinity of AH11110A for prejunctional .alpha.2-adrenoceptors in rabbit vas deferens (pA2=5.44) was not much lower than that displayed for .alpha.1-adrenoceptor subtypes, revealing that AH11110A, besides .alpha.1-adrenoceptors, also interacts with .alpha.2-adrenoceptors, and thus may be unsuitable for .alpha.-adrenoceptor subtype characterization,

L14 ANSWER 19 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
at least in smooth muscle contg. functional studies.
IT 21102-95-4, RMY 7378
RL: BAC (Biological activity or effector, except adverse); BFR
(Biological process); BSU (Biological study, unclassified); BIOL (Biological study);
PROC (Process)
(failure of AH1110A to functionally discriminate between
.alpha.1-adrenoceptor subtypes A, B and D or between .alpha.1- and
.alpha.2-adrenoceptors in animal tissues as compared with other
agents)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



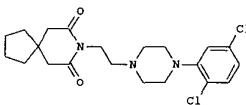
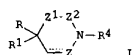
● 2 HCl

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:63974 CAPLUS
DOCUMENT NUMBER: 134:115867
TITLE: Preparation of azaspirodecane(di)ones and analogs
as
.alpha.1D adrenoceptor antagonists
INVENTOR(S): Leonardi, Amadeo; Barlocco, Daniela; Motta,
Gianni;
TESTA, Rodolfo
PATENT ASSIGNEE(S): Recordati Industria Chimica e Farmaceutica S.p.A.,
Italy; Recordati S.A., Chemical and Pharmaceutical
Company
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-------------------|------------|
| WO 2001005765 | A1 | 20010125 | WO 2000-EP6738 | 20000714 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| IT 99M11578 | A1 | 20010115 | IT 1999-M11578 | 19990715 |
| EP 1200406 | A1 | 20020502 | EP 2000-945917 | 20000714 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | |
| PRIORITY APPLN. INFO.: | | | IT 1999-M11578 | A 19990715 |
| | | | WO 2000-EP6738 | W 20000714 |
| OTHER SOURCE(S): | | | MARPAT 134:115867 | |
| G1 | | | | |

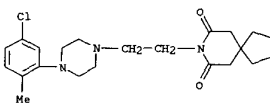
L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



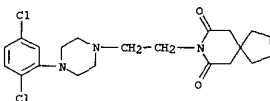
AB Title compds. [I; R,R1 = H or alkyl; RR1 = (CH2)2-6; R4 = CHR3CHR7CHR3; R3 = H or alkyl; R7 = Z3Z4R2; R2 = halo, alkyl, cyano; Z = CH2, CO, CH; Z1 = bond or CH2; Z2 = CH2 or CO; Z3 = piperidine- or -azine-1,4-diyl or NMe(CH2)mZ5Z4R2; Z4 = (un)substituted 1,2-phenylene; Z5 = O, S, NH, NMe; m = 2-4; dashed line = optional addnl. bond] were prep'd. Thus, 8-(2-bromoethyl)-8-azaspiro[4.5]decane-7,9-dione was aminated by 1-(2,5-dichlorophenyl)piperazine to give title compd. II. Data for biol.

activity of I were given.
IT 255893-42-6P 321601-67-6P 321601-68-7P
321601-69-8P 321601-70-1P 321601-71-2P
321601-72-3P 321601-73-4P 321601-74-5P
321601-75-6P 321601-76-7P 321601-77-8P
321601-78-9P 321601-79-0P 321601-80-3P
321601-81-4P 321601-82-5P 321601-83-6P
321601-84-7P 321601-87-0P 321601-89-2P
321601-90-5P 321601-91-6P 321601-92-7P
321601-93-8P 321601-94-9P 321601-95-0P
321601-96-1P 321601-97-2P 321602-28-2P
321602-36-2P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of azaspirodecane(di)ones and analogs as .alpha.1D
adrenoceptor antagonists)
RN 255893-42-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(5-chloro-2-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

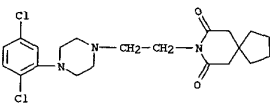


RN 321601-67-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 321601-68-7 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-
piperazinyl]ethyl]-, monomethanesulfonate (9CI) (CA INDEX NAME)

CM 1
CRN 321601-67-6
CMF C21 H27 C12 N3 O2



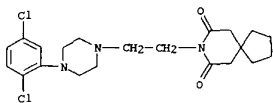
CM 2
CRN 75-75-2
CMF C H4 O3 S



RN 321601-69-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]-, dimethanesulfonate (9CI) (CA INDEX NAME)

CM 1

CRN 321601-67-6
CMF C21 H27 Cl2 N3 O2



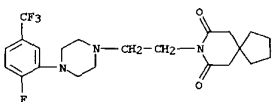
CM 2

CRN 75-75-2
CMF C H4 O3 S

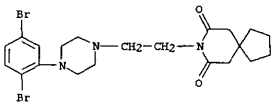


RN 321601-70-1 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

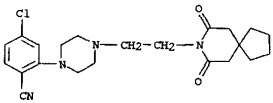
RN 321601-74-5 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-[2-fluoro-5-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



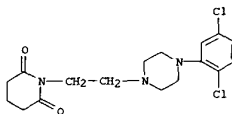
RN 321601-75-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dibromophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



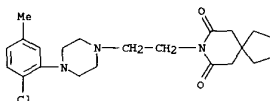
RN 321601-76-7 CAPLUS
CN Benzonitrile, 4-chloro-2-[4-[2-(7,9-dioxo-8-azaspiro[4.5]dec-8-yl)ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



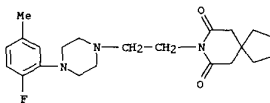
RN 321601-77-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



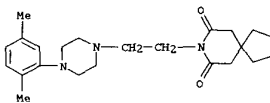
RN 321601-71-2 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



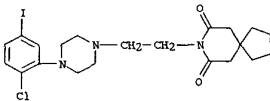
RN 321601-72-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-fluoro-5-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



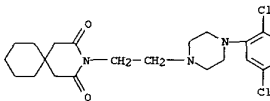
RN 321601-73-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



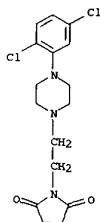
RN 321601-78-9 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-iodophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



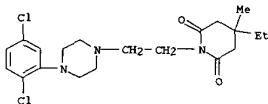
RN 321601-79-0 CAPLUS
CN 3-Azaspiro[5.5]undecane-2,4-dione, 3-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



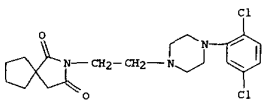
RN 321601-80-3 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 321601-81-4 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]-4-ethyl-4-methyl- (9CI) (CA INDEX NAME)

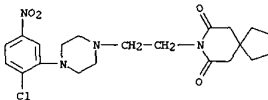


RN 321601-82-5 CAPLUS
CN 2-Azaspiro[4.4]nonane-1,3-dione, 2-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

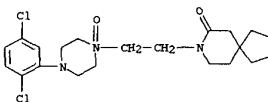


RN 321601-83-6 CAPLUS
CN 7-Azaspiro[3.5]nonane-6,8-dione, 7-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

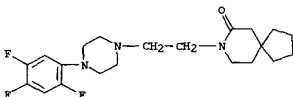
L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-chloro-5-nitrophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



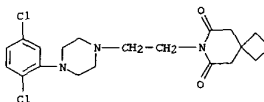
RN 321601-91-6 CAPLUS
CN 8-Azaspiro[4.5]decane-7-one, 8-[2-[4-(2,5-dichlorophenyl)-1-oxido-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



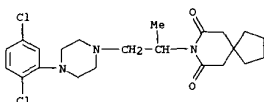
RN 321601-92-7 CAPLUS
CN 8-Azaspiro[4.5]decane-7-one, 8-[2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



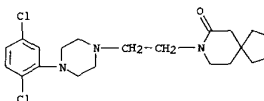
RN 321601-93-8 CAPLUS
CN 3-Azaspiro[5.5]undecan-2-one, 3-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



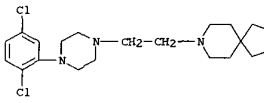
RN 321601-84-7 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)



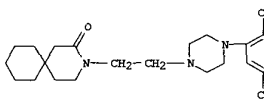
RN 321601-87-0 CAPLUS
CN 8-Azaspiro[4.5]decane-7-one, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



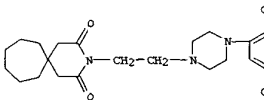
RN 321601-89-2 CAPLUS
CN 8-Azaspiro[4.5]decane,
8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



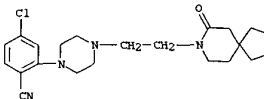
RN 321601-90-5 CAPLUS



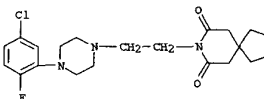
RN 321601-94-9 CAPLUS
CN 3-Azaspiro[5.6]dodecane-2,4-dione, 3-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



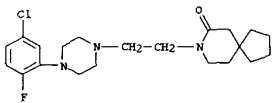
RN 321601-95-0 CAPLUS
CN Benzonitrile,
4-chloro-2-[4-[2-(7-oxo-8-azaspiro[4.5]dec-8-yl)ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



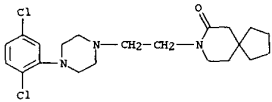
RN 321601-96-1 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(5-chloro-2-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 321601-97-2 CAPLUS
 CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(5-chloro-2-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

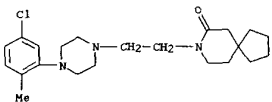


RN 321602-28-2 CAPLUS
 CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(2,5-dichlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



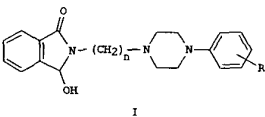
● HCl

RN 321602-36-2 CAPLUS
 CN 8-Azaspiro[4.5]decan-7-one, 8-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



IT 321602-22-6P 321602-24-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT (Reactant or reagent)
 (prepn. of azaspirodecane(dione)s and analogs as α -1D
 adrenoceptor
 antagonists)

L14 ANSWER 21 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000;780228 CAPLUS
 DOCUMENT NUMBER: 134;71569
 TITLE: Preparation of N-[ω -(4-aryl-1-piperazinyl)ethyl/propyl]-3-hydroxyphthalimides
 AUTHOR(S): Desai, R. A.; Samant, S. D.
 CORPORATE SOURCE: Organic Chemistry Research Laboratory, University
 Department of Chemical Technology, Mumbai, 400
 019,
 SOURCE: India
 Indian Journal of Chemistry, Section B: Organic
 Chemistry Including Medicinal Chemistry (2000),
 39B(6), 455-457
 CODEN: IJUSBU; ISSN: 0376-4699
 PUBLISHER: National Institute of Science Communication, CSIR
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 134;71569
 GI

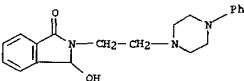


AB The reaction of ω -(4-aryl-1-piperazinyl)ethyl/propyl amine with 3-hydroxyphthalide furnishes the title compds. I (n = 2, 3; R = H, 2-, 3-,

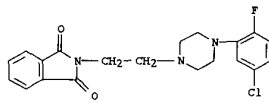
4-Me, Cl) along with minor amts. of the corresponding N-[ω -(4-aryl-1-piperazinyl)ethyl/propyl]-2-formylbenzamides.

IT 316146-14-2P 316146-15-3P 316146-17-5P
 316146-20-0P 316146-22-2P 316146-24-4P
 316146-26-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)

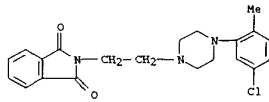
RN 316146-14-2 CAPLUS
 CN 1H-Indolol-1-one, 2,3-dihydro-3-hydroxy-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 20 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 321602-22-6 CAPLUS
 CN 1H-Indolol-1,3(2H)-dione, 2-[2-[4-(5-chloro-2-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

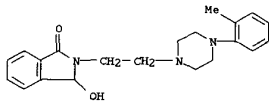


RN 321602-24-8 CAPLUS
 CN 1H-Indolol-1,3(2H)-dione, 2-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

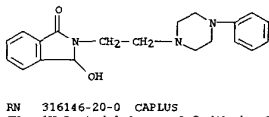


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

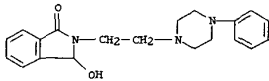
L14 ANSWER 21 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 316146-15-3 CAPLUS
 CN 1H-Indolol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



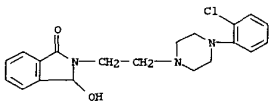
RN 316146-17-5 CAPLUS
 CN 1H-Indolol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(3-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



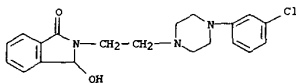
RN 316146-20-0 CAPLUS
 CN 1H-Indolol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



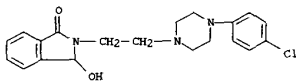
RN 316146-22-2 CAPLUS
 CN 1H-Indolol-1-one, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)



L14 ANSWER 21 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 316146-24-4 CAPLUS
CN 1H-Isindol-1-one, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)



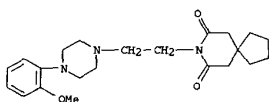
RN 316146-26-6 CAPLUS
CN 1H-Isindol-1-one, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-2,3-dihydro-3-hydroxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 22 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:779744 CAPLUS
DOCUMENT NUMBER: 134:857
TITLE: An .alpha.1A/.alpha.1L-adrenoceptor mediates contraction of canine subcutaneous resistance arteries
AUTHOR(S): Argyle, Sally Anne; McGrath, John Christie
CORPORATE SOURCE: Autonomic Physiology Unit, Division of Neuroscience and Biomedical Systems, Institute of Biomedical & Life Sciences, University of Glasgow, Glasgow, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 295(2), 627-633
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB To det. the characteristics of the .alpha.1-adrenoceptor subtypes involved in adrenergic regulation of peripheral vascular resistance, contraction of canine s.c. resistance arteries was studied using wire myographs. The potencies of agonists and antagonists, chosen for their ability to discriminate between .alpha.1-adrenoceptor subtypes, were assessed in the presence of cocaine (3 .mu.M), corticosterone (30 .mu.M), and propranolol (1 .mu.M). The rank order of agonist potency (pEC50 +/- S.E.) was (R)-A-61603 (7.88 +/- 0.1) > norepinephrine (6.41 +/- 0.1) > phenylephrine (5.83 +/- 0.1). The high sensitivity to (R)-A-61603 relative to phenylephrine is inconsistent with the presence of the .alpha.1D-adrenoceptor and most consistent with an .alpha.1A-adrenoceptor response. This is supported by the low affinity for the .alpha.1D-selective antagonist RMY 7378 (pKB 6.51 +/- 0.47). The low pA2 values for prazosin (8.36) and HV723 (8.81), by definition, indicate the involvement of the putative .alpha.1L-adrenoceptor, a hypothesis supported by the pA2 values for WB4101 (8.42) and 5-methyl-urapidil (8.08). Pre-exposure to 1 .mu.M CEC had little effect, whereas 100 .mu.M CEC reduced the max. contraction but not the sensitivity to norepinephrine. This low sensitivity to CEC argues against the presence of the .alpha.1B-adrenoceptor. We conclude that, by current definitions, an .alpha.1A-/.alpha.1L-adrenoceptor causes contraction of these vessels. This does not support the concept that selectivity for the .alpha.1A-adrenoceptor is the basis for the effectiveness of some .alpha.1-blockers in some tissues, such as prostate, but not in other tissues such as blood vessels. Rather, the generally low potency of .alpha.1-blockers in some tissues may be due to a tissue-specific property

L14 ANSWER 22 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
of the receptors.
IT 21102-95-4, RMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.1A/.alpha.1L-adrenoceptor mediates contraction of canine s.c. resistance arteries)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

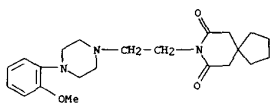


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REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 23 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:757753 CAPLUS
DOCUMENT NUMBER: 134:51220
TITLE: Pharmacological characterization of [3H]-JTH-601, a novel .alpha.1-adrenoceptor antagonist binding to recombinant human .alpha.1-adrenoceptors and human prostates
AUTHOR(S): Kanamaru, Hiroshi; Okada, Kenichiro; Muramatsu, Ikunobu
CORPORATE SOURCE: Department of Pharmacology, School of Medicine, Fukui Medical University, Fukui, 910-1193, Japan
SOURCE: Life Sciences (2000), 67(20), 2443-2451
CODEN: LIFSAK; ISSN: 0024-3205
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several .alpha.1-adrenoceptor (AR) selective antagonists are now widely used to improve lower urinary tract symptoms in benign prostatic hyperplasia patients. However, these drugs often result in orthostatic hypotension, because of their poor uroselectivity; the blockade of .alpha.1-AR not only in prostate but also in vasculature. Here we have investigated uroselectivity of JTH-601, a newly developed antagonist, in radioligand binding expt. using recombinant human .alpha.1-AR subtypes and human prostate. In satn. expts., [3H]-JTH-601 showed subtype selectivity: high affinity to .alpha.1a-AR (pKd; 9.88 +/- 0.09), lower affinity to .alpha.1b-AR (pKd; 8.96 +/- 0.17) and no specific binding at concns. up to 3000 pM to .alpha.1d-AR. In competition expts., JTH-601 and its metabolic compd. (JTH-601-G1) also showed .alpha.1a-AR selectivity, exhibiting approx. 5 times higher affinity for .alpha.1a-AR than for .alpha.1b-AR, 10 to 20 times higher affinity than for .alpha.1d-AR, resp. [3H]-JTH-601 also bound to human prostate membranes in monophasic manner with high affinity const. (pKd; 9.89 +/- 0.12, Bmax=123.6 +/- 16 fmol/mg protein). JTH-601 is a unique .alpha.1-AR antagonist that shows high affinity and selectivity for human recombinant .alpha.1a- and human prostate. This new compd. is useful for understanding .alpha.1-AR pharmacol. and may have a therapeutic value.
IT 21102-95-4, RMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

L14 ANSWER 23 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 (pharmacol. characterization of [3H]-JTH-601, a novel
 .alpha.1-adrenoceptor antagonist binding to recombinant human
 .alpha.1-adrenoceptors and human prostates)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

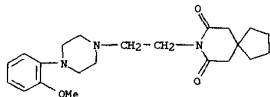


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REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 24 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:719190 CAPLUS
 DOCUMENT NUMBER: 133:344153
 TITLE: Development of scintillation-proximity assays for
 alpha adrenoceptors
 AUTHOR(S): Gobel, J.; Saussy, D. L.; Goetz, A. S.
 CORPORATE SOURCE: Department of Receptor Biochemistry, Glaxo
 Wellcome
 NC, Research and Development, Research Triangle Park,
 27709, USA
 SOURCE: Journal of Pharmacological and Toxicological
 Methods
 (1999), 42(4), 237-244
 CODEN: JPTMEZ; ISSN: 1056-8719
 PUBLISHER: Elsevier Science Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Binding assays have long been used to det. compd. affinity and
 selectivity
 for various seven-transmembrane receptors. Over time, the degree of
 complexity has significantly reduced, whereas the throughput of the
 various assays has greatly increased. In this article, the authors
 detail the development of a filter-binding assay and a
 scintillation-proximity
 assay (SPA) designed to quantify a compd.'s affinity for the three
 .alpha.1-adrenoceptor subtypes, .alpha.1A, .alpha.1B, and .alpha.1D.
 The various components of the assays such as ease of assay performance,
 robustness, cost, and generation of radioactive waste are compared and
 contrasted. On the basis of the results, the SPA offers many
 advantages of high-throughput assay formats over the traditional filter-binding
 assay. To follow up on the success of the .alpha.1-adrenoceptor SPA,
 SPAs for the three .alpha.2-adrenoceptors were developed and are detailed
 in this article. Affinity data generated for a select no. of .alpha.2
 compds. agree with reported literature values. These assays, like
 those for .alpha.1 subtypes, are very amenable to high-throughput screening
 campaigns. In conclusion, scintillation-proximity assays offer
 significant advantages over filter-binding assays.
 IT 21102-95-4, RMY 7378
 RL: ANT (Analyte); BPR (Biological process); BSU (Biological study,
 unclassified); ANST (Analytical study); BIOL (Biological study); PROC
 (Process)
 (scintillation-proximity assays to quantify compd.'s affinity for
 alpha adrenoceptor subtypes)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 24 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

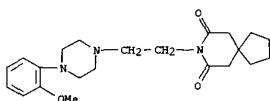


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REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 25 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:667305 CAPLUS
 DOCUMENT NUMBER: 133:359442
 TITLE: .alpha.1-Adrenoceptors in the guinea pig thoracic
 aorta
 AUTHOR(S): Yamamoto, Yoshihisa; Koike, Katsuo
 CORPORATE SOURCE: Department of Chemical Pharmacology, Toho
 University
 School of Pharmaceutical Sciences, Chiba,
 274-8510,
 Japan
 SOURCE: Journal of Smooth Muscle Research (1999), 35(5,6),
 181-192
 CODEN: JSMRE2; ISSN: 0916-8737
 PUBLISHER: Japanese Society of Smooth Muscle Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In the present study, the authors tried to det. which .alpha.1-
 adrenoceptor subtypes are involved in the guinea pig thoracic aorta by
 using in vitro functional anal. Firstly, the authors tried to est.
 the pA2 values of some key .alpha.1-adrenoceptor antagonists (prazosin,
 5-methylurapidil, WB4101, BMV7378 and tamsulosin) against responses to
 norepinephrine in the thoracic aorta of guinea pigs. The
 concn.-response
 curves of norepinephrine were rightward shifted by the presence of
 prazosin, 5-methylurapidil, WB4101, BMV7378 and tamsulosin. The pA2
 values for these antagonists against norepinephrine were 7.83, 7.78,
 8.20,
 5.73 and 9.57, resp. Secondly, the authors tried to compare the
 estd. pA2
 values obtained in the present study with reported pKi and pA2 values
 for cloned and native .alpha.1-adrenoceptor subtypes. In rabbit
 mesenteric
 artery, trigone, urethra, prostate and human lower urinary tract which
 were proposed to contain the putative .alpha.1L-adrenoceptor, the
 authors obtained a good correlation for the pA2 values reported in these
 tissues
 with pA2 values estd. in guinea pig thoracic aorta. Moreover,
 regression
 lines were close to the line of identity. These results suggest that
 the .alpha.1-adrenoceptors mediating contraction of guinea pig thoracic
 aorta are similar pharmacol. to the putative .alpha.1L-adrenoceptor subtype
 in rabbit mesenteric artery, trigone, urethra, prostate and human lower
 urinary tract. As a final point, guinea pig thoracic aorta may be
 used as
 a tool to develop new .alpha.1-adrenoceptor antagonists
 therapeutically
 advantageous in the treatment of urinary tract obstruction (e.g., in
 benign prostatic hyperplasia).
 IT 21102-95-4, RMY7378
 RL: RAC (Biological activity or effector, except adverse); BSU
 (Biological)

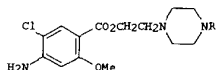
L14 ANSWER 25 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 study, unclassified); BIOL (Biological study)
 (.alpha.1-adrenoceptor antagonists; .alpha.1-adrenoceptor subtypes
 mediating vasoconstriction in guinea pig thoracic aorta)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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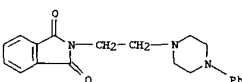
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 26 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:653172 CAPLUS
 DOCUMENT NUMBER: 133:362752
 TITLE: New Arylpiperazine Derivatives as Antagonists of
 the Human Cloned 5-HT4 Receptor Isoforms
 AUTHOR(S): Curtet, Sophie; Soulier, Jean-Louis; Zahradnik,
 Ivan; Giner, Mireille; Berque-Bestel, Isabelle; Milet,
 Jeanne; Lezoualc'h, Frank; Donzeau-Gouge, Patrick;
 Sicsic, Sames; Fischmeister, Rodolphe; Langlois,
 Michel
 CORPORATE SOURCE: INSERM U-446 Institut de Signalisation et
 Innovation
 de
 SOURCE: Paris-Sud, Chatenay-Malabry, 92296, Fr.
 Journal of Medicinal Chemistry (2000), 43(20),
 3761-3769
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 133:362752
 GI



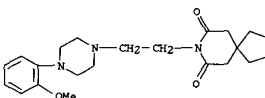
AB New derivs. of arylpiperazine I [R = (un)substituted Ph, 1-naphthyl,
 CO2Et, CO2CMe3, Me, H, pyrimidinyl, pyrazinyl, pyridazinyl,
 pyridinyl]
 were designed from ML 10302, a potent 5-HT4 receptor agonist in the
 gastrointestinal system. I were synthesized by condensation of the
 arylpiperazines or heteroaryl piperazines with 2-bromomethyl
 4-amino-5-chloro-2-methoxybenzoate. I were evaluated in binding
 assays on
 the recently cloned human 5-HT4(e) isoform stably expressed in C6
 glial cells with [3H]GR 113808 as the radioligand. The affinity values (Ki)
 depended upon the substituent on the arom. ring. A chlorine atom
 produced
 a marked drop in activity (Ki > 100 nM), while a m-methoxy group gave
 a
 compd. with nanomolar affinity (Ki = 3 nM). The most potent compds.
 were
 the heterocyclic derivs. with pyrimidine, pyrazine, pyridazine, or
 pyridine moieties. Ki values for I [R = Ph, 2-pyrimidinyl] were
 detd. for

L14 ANSWER 26 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 the 5-HT4(a), 5-HT4(b), 5-HT4(c), and 5-HT4(d) receptor isoforms
 transiently expressed in COS cells. The results indicated that the
 compds. were not selective. They produced an inhibition of the
 5-HT-stimulated cAMP synthesis in the C6 glial cells stably
 expressing the
 5-HT4(e) receptor and shifted the 5-HT concn.-effect curve on
 adenylyl
 cyclase activity with pKD values of 7.44 and 8.47, resp. In isolated
 human atrial myocytes, I [R = 2-pyrimidinyl] antagonized the
 stimulatory
 effect of 5-HT on the L-type calcium current (ICa) with a KD value
 of 0.7
 nM.
 IT 75000-24-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
 RACT
 (Reactant or reagent)
 cloned
 (arylpiperazinylethyl) aminobenzoates as antagonists of the human
 5-HT4 receptor isoforms)
 RN 75000-24-7 CAPLUS
 CN 1H-Indole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-
 (9CI) (CA INDEX NAME)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 27 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:565500 CAPLUS
 DOCUMENT NUMBER: 134:25262
 TITLE: Effects of the 5HT1A agonist/antagonist RMY 7378
 on
 light-induced phase advances in hamster circadian
 activity rhythms during aging
 AUTHOR(S): Byku, Mirnela; Gannon, Robert L.
 CORPORATE SOURCE: Department of Biology, Dowling College, Oakdale,
 NY,
 11769, USA
 SOURCE: Journal of Biological Rhythms (2000), 15(4),
 300-305
 CODEN: JBRHEE; ISSN: 0748-7304
 PUBLISHER: Sage Science Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB RMY 7378 was a highly effective chronobiotic that more than doubled
 the
 magnitude of light-induced phase shifts in hamster wheel-running
 activity
 rhythms. Light-induced phase advances of .gtoreq.6 h in hamster
 wheel-running activity following a single systemic dose of RMY 7378
 were
 obsd. Furthermore, the RMY 7378 potentiation of phase shifts was
 maintained in old hamsters, suggesting that RMY 7378 has a different
 site
 of activity than that of previously reported 5HT1A agonists that have
 a
 diminished effect on circadian phase during aging.
 IT 21102-95-4, RMY 7378
 RL: RAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); BIOL (Biological study)
 (serotoninerigic1A agonist/antagonist RMY 7378 effect on
 light-induced
 phase advances in circadian activity during aging)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



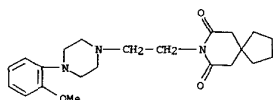
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REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR
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L14 ANSWER 27 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 28 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:558944 CAPLUS
DOCUMENT NUMBER: 133:276210
TITLE: Tissue selectivity of XMD-3213, an
.alpha.1-adrenoceptor antagonist, in human
prostate
and vasculature
AUTHOR(S): Murata, Satoshi; Taniguchi, Takanobu; Takahashi,
Masahiko; Okada, Kenichiro; Akiyama, Katsuyoshi;
Muramatsu, Ikunobu
CORPORATE SOURCE: Department of Pharmacology and Urology, School of
Medicine, Fukui Medical University, Matsuoka,
Japan
SOURCE: Journal of Urology (Baltimore) (2000), 164(2),
578-583
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We evaluated the binding and functional affinity of XMD-3213 and other
.alpha.1-adrenoceptor (AR) antagonists such as prazosin or
tamsulosin, to
compare the tissue selectivity of these antagonists between human
prostate
and vasculature. In the binding expts., satn. expts. using [3H]-XMD
and
[3H]-prazosin (PZ) were performed, and competition of [3H]-PZ binding
by
antagonists was also examd. in human prostatic and aortic membranes.
In
the functional study, contractile responses to noradrenaline were
evaluated in human prostate and mesenteric artery. [3H]-PZ bound to
human
prostatic and aortic membranes with subnanomolar affinity. [3H]-XMD
also
bound to human prostate, with higher affinity than [3H]-PZ; whereas
it did
not bind sufficiently to human aorta. Competition of [3H]-PZ binding
revealed that XMD-3213 had more than 200-fold higher affinity for
human
prostate than for aorta. Binding profiles of antagonists revealed
that
human prostate predominantly expressed .alpha.1A-AR, whereas human
aorta
expressed .alpha.1B-AR mainly. In functional expts., XMD-3213
potently
inhibited the noradrenaline-induced contraction in human prostate as
potently as tamsulosin, although prazosin showed relatively low
affinity.
Comparing these functional affinities with those in the mesenteric
artery,
only XMD-3213 exhibited substantial tissue selectivity, showing more
than
100-fold higher affinity for human prostate than for mesenteric
artery.
Functional affinity of each antagonist suggested that noradrenaline-
induced contractions were mainly mediated by .alpha.1L-AR in the human

L14 ANSWER 28 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
prostate and by .alpha.1B-AR in the mesenteric artery. These results
suggest that XMD-3213 is a substantially prostate-selective
.alpha.1-AR
antagonist in human tissues compared with other .alpha.1-AR
antagonists.
IT 21102-95-4, RMY7378
RL: BAC (Biological activity or effector, except adverse); BPR
(Biological
process); BSU (Biological study, unclassified); BIOL (Biological
study);
PROC (Process)
(tissue selectivity of XMD-3213 and other .alpha.1-adrenoceptor
antagonists in human prostate and vasculature)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



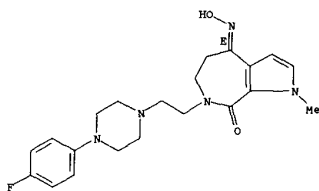
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REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE
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RECORD. ALL CITATIONS AVAILABLE IN THE RE
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L14 ANSWER 29 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:554947 CAPLUS
DOCUMENT NUMBER: 133:281710
TITLE: Studies on antihypertensive agents with
antithrombotic
activity. 2. Syntheses and pharmacological
evaluation
of pyrrolo[2,3-c]azepine derivatives
AUTHOR(S): Mizuno, Akira; Miya, Mikiko; Kamei, Tomoe;
Shibata,
Takiguchi,
Chikako; Hidaka, Toshinori; Yamaki, Akira;
Inomata,
Norio
CORPORATE SOURCE: Suntory Institute for Biomedical Research, Osaka,
618-8503, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48(8),
1129-1137
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of 7-aminoalkylpyrrolo[2,3-c]azepine derivs. was synthesized
and
evaluated as .alpha.1-adrenergic and 5-HT2 receptor antagonists, with
the
aim of finding a novel potent antihypertensive agent with both
activities.
Among the compds. obtained in this study, (E)-1-ethyl-7-[3-[4-(4-
fluorophenyl)piperazin-1-yl]propyl]-4-hydroxyimino-1,4,5,6,7,8-
hexahydro-2H-pyrrolo[2,3-c]azepin-8-one (1) displayed potent
.alpha.1-adrenoceptor blocking activity (pA2 = 7.83 +/- 0.20) and
5-HT2-receptor blocking activity (pA2 = 9.47 +/- 0.17) in isolated
guinea
pig arteries. At 3 mg/kg oral administration, 1 exhibited
antihypertensive activity more potent than that of doxazosin in
deoxycorticosterone acetate (DOCA)-salt hypertensive dogs.
Furthermore,
this compd. reduced the rate of mouse acute pulmonary thromboembolic
death induced by collagen and serotonin at oral doses of 0.3 mg/kg or
more, and its effect lasted for at least 6 h at 3 mg/kg.
IT 300548-34-9P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(prepn. of aminoalkylpyrroloazepinediones with .alpha.-adrenergic
and
5-HT2 antagonist activity)
RN 300548-34-9 CAPLUS
CN Pyrrolo[2,3-c]azepine-4,8(1H,5H)-dione, 7-[2-[4-(4-fluorophenyl)-1-
piperazinyl]ethyl]-6,7-dihydro-1-methyl-, 4-oxime, (4E)- (9CI) (CA
INDEX
NAME)

Double bond geometry as shown.

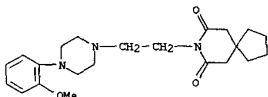
L14 ANSWER 29 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 30 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:536311 CAPLUS
DOCUMENT NUMBER: 134:157934
TITLE: Quantitative imaging in live human cells reveals intracellular .alpha.1-adrenoceptor ligand-binding sites
AUTHOR(S): Mackenzie, Janet F.; Daly, Craig J.; Fediani, John D.;
CORPORATE SOURCE: McGrath, John C.
Neuroscience Autonomic Physiology Unit, Division of and Biomedical Systems, Institute of Biomedical & Life Sciences, University of Glasgow, Glasgow, UK
SOURCE: Journal of Pharmacology and Experimental Therapeutics
(2000), 294(2), 434-443
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Cellular distribution and binding characteristics of native .alpha.1-adrenoceptors (ARs) were detd. in a live, single, human smooth muscle cell (SMC) with confocal laser scanning microscopy and a fluorescent ligand, BODIPY-FL prazosin (QAPB). This allowed single-cell competitive ligand binding and showed that 40% of .alpha.1-AR-binding sites in native cells are intracellular. QAPB had high affinity and acted as a nonselective, competitive antagonist vs. [3H]prazosin at cloned human .alpha.1a-, .alpha.1b-, and .alpha.1d-AR subtypes on membrane preps. and whole cells. RS100329 had 70-fold selectivity for .alpha.1a-ARs vs. .alpha.1b- and .alpha.1d-ARs, validating its use to identify this subtype. In similar cells QAPB-assocd. fluorescence provided quant. data analogous and comparable to [3H]prazosin binding in whole cells. In human, dissocd., prostatic smooth muscle cells QAPB-assocd. fluorescence binding exhibited specific high-affinity binding properties (FKD = 0.63 +/- 0.02 nM), which was 3- to 4-fold higher compared with recombinant cells (FKD = 2.1-2.3 nM). Internal consistency in the data showed that affinity is greater, in general, in membrane preps. than in cells but also greater in the native prostatic tissues or cells than in equiv. recombinant receptors. Fluorescence revealed binding sites both on the plasmalemmal membrane and on intracellular compartments: at all locations RS100329 inhibited QAPB binding identifying the sites as .alpha.1a-ARs. Quant. three-dimensional mapping of QAPB-assocd. fluorescence binding in native

L14 ANSWER 30 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
human cells showed that 40% of high-affinity-binding sites in intracellular compartments. This provides a potential new site for physiol. agonism and makes intracellular access a potential differentiator of drug action.
IT 21102-95-4, RMY7378
RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.1-adrenoceptor ligand-binding sites are intracellularly localized in live human prostatic smooth muscle cells)
RN 21102-95-4 CAPLUS
CN 8-Azaspipiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

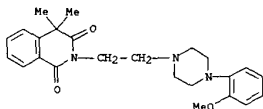


●2 HCl

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 31 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:458289 CAPLUS
DOCUMENT NUMBER: 133:130140
TITLE: Characterization of the .alpha.2-adrenoceptor subtype, which functions as .alpha.2-autoreceptor in human neocortex
AUTHOR(S): Feuerstein, Thomas J.; Huber, Boris; Vetter, Jan; Aranda, Heike; Van Velthoven, Vera; Limberger, Norbert
CORPORATE SOURCE: Sektion Klinische Neuropharmakologie der Neurologischen Universitätsklinik, Freiburg, D-79106,
Germany
SOURCE: Journal of Pharmacology and Experimental Therapeutics
(2000), 294(1), 356-362
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The pharmacol. properties of the .alpha.2-adrenergic receptors regulating the release of norepinephrine were investigated in human neocortex. Slices were preincubated with [3H]norepinephrine, superfused under blockade of transmitter reuptake, and stimulated elec. First, the autoinhibitory circuit of [3H]norepinephrine release was analyzed quant. by estn. of the Kd of norepinephrine at the .alpha.2-autoreceptor (10-7.59 M), the concn. of the endogenous transmitter causing this autoinhibition at a stimulation frequency of 3 Hz (10-7.61 M), and the max. inhibition obtainable through the autoreceptor (83%). Second, antagonist pKb values of nine antagonists were detd. by using their pEC50 values (neg. logarithms of antagonist concns. that increased the elec. evoked overflow of tritium by 50%) against the release-inhibiting effect of the endogenous transmitter. When compared with binding or functional data from the literature, the pKb values correlated best with the antagonist affinities at .alpha.2A binding sites. In contrast, the correlations with .alpha.2B, .alpha.2C, and .alpha.2D sites were not as good. It is concluded that in human neocortex prejunctional autoreceptors are .alpha.2A.
IT 67339-62-2, ARC239
RI: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(norepinephrine release from human neocortex and calcn. of unbiased

L14 ANSWER 31 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
disocn. consts. of antagonists in relation to characterization of
.alpha.2-adrenoceptor subtype which functions as
.alpha.2-autoreceptor
in human neocortex)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

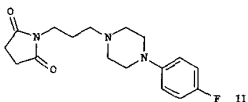


REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 32 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:455295 CAPLUS
DOCUMENT NUMBER: 133:89543
TITLE: Preparation of 1-[3-(2,5-dioxopyrrolidino- or
2,6-dioxopiperidino)propyl]-4-aryl piperazines and
analogs as uroselective .alpha.1-adrenoceptor
antagonists
INVENTOR(S): Anand, Nitya; Sinha, Neelima; Jain, Sanjay; Mehta,
Anitar Bahadurupda, Jang
PATENT ASSIGNEE(S): Ranbaxy Laboratories Limited, India
SOURCE: U.S., 10 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

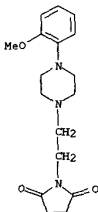
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 6083950 | A | 20000704 | US 1998-120265 | 19980721 |
| US 6090809 | A | 20000718 | US 1998-203855 | 19981202 |
| WO 2000005206 | A1 | 20000203 | WO 1999-1B140 | 19990126 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TH, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9919797 | A1 | 20000214 | AU 1999-19797 | 19990126 |
| WO 2000005205 | A1 | 20000203 | WO 1999-1B1296 | 19990716 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GE, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TH, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9946410 | A1 | 20000214 | AU 1999-46410 | 19990716 |

L14 ANSWER 32 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
BR 9912318 A 20010502 BR 1999-12318 19990716
EP 1097134 A1 20010509 EP 1999-929633 19990716
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
US 6410735 B1 20020625 US 2000-578088 20000524
US 6420366 B1 20020716 US 2000-577788 20000524
US 6420559 B1 20020716 US 2000-577789 20000524
PRIORITY APPLN. INFO.: IN 1997-DE3260 A 19971113
IN 1997-DE3261 A 19971113
US 1998-120265 A3 19980721
US 1999-1R140 W 19990126
WO 1999-1B1296 W 19990716
OTHER SOURCE(S): MARPAT 133:89543
GI



AB Title compds., e.g., R(CH2)nCH2CH2CH2R1 [I; R = 2,5-dioxopyrrolidino, 2,6-dioxopiperidino, etc.; R1 = (un)substituted 2-pyridinyl, -2-pyrimidinyl, -Ph; R3 = H, OH, alkyl, alkoxy; Z = piperidine- or piperazine-1,4-diyl; n = 0-4] were prepd. Thus, 2,5-dioxopyrrolidino was N-alkylated by 1-(3-chloropropyl)-4-(4-fluorophenyl)piperazine to give title compd. II. Data for biol. activity of I were given.
IT 255861-61-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of 1-[3-(2,5-dioxopyrrolidino- or 2,6-dioxopiperidino)propyl]-4-aryl piperazines and analogs as uroselective .alpha.1-adrenoceptor antagonists)
RN 255861-61-1 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

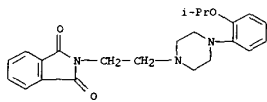
L14 ANSWER 32 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

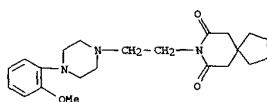
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 33 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:379674 CAPLUS
 DOCUMENT NUMBER: 133:150523
 TITLE: Novel arylpiperazines as selective .alpha.1-adrenergic receptor antagonists
 AUTHOR(S): Li, Xiaobing; Murray, William V.; Jolliffe, Linda; Pulito, Virginia
 CORPORATE SOURCE: The R. W. Johnson Pharmaceutical Research Institute,
 SOURCE: San Diego, CA, 92121, USA
 BIOORGANIC & MEDICINAL CHEMISTRY LETTERS (2000), 10(10), 1093-1096
 CODEN: BMCLB; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A novel series of arylpiperazines has been synthesized and identified as antagonists of .alpha.1a adrenergic receptor (.alpha.1a-AR) implicated in benign prostatic hyperplasia. These compds. selectively bind to membrane bound .alpha.1a-AR with K_is as low as 0.66 nM. As such, these potentially represent a viable treatment for BPH without the side effects associated with known .alpha.1-adrenergic antagonists.
 IT 216252-67-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of arylpiperazines as selective .alpha.1-adrenergic receptor antagonists)
 RN 216252-67-4 CAPLUS
 CN 1H-Indole-1,3(2H)-dione, 2-[2-[4-(2-(1-methylethoxy)phenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 34 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 results indicate that quant. pharmacol. can be studied successfully in single cells even though equil. could not be achieved in the agonist-antagonist-response relationship in this particular cell phenotype. The study also showed a form of fade that could be readily explained.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (single-cell recombinant pharmacol. of bovine .alpha.1a-adrenoceptor in rat-1 fibroblasts and intracellular calcium release)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



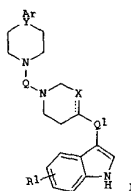
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REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 34 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:373728 CAPLUS
 DOCUMENT NUMBER: 133:84624
 TITLE: Single-cell recombinant pharmacology: bovine .alpha.1a-adrenoceptors in rat-1 fibroblasts
 release intracellular Ca²⁺, display subtype-characteristic agonism and antagonism, and exhibit an antagonist-reversible inverse
 concentration-response phase
 AUTHOR(S): Pediani, John Daniel; Mackenzie, Janet Fraser; Heeley, Robert Paul; Daly, Craig James; Mograth, John
 CHRISTIE
 CORPORATE SOURCE: Autonomic Physiology Unit, Division of Neuroscience and Biomedical Systems, Institute of Biomedical Life Sciences, University of Glasgow, Glasgow, UK
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (2000), 293(3), 887-895
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Phenylephrine (Phe)-activated Ca²⁺ signals recorded from single rat-1 fibroblasts stably expressing the bovine .alpha.1a-adrenoceptor (AR) were characterized and used to analyze functional agonist-antagonist interactions. The response to Phe was initiated by the mobilization of stored Ca²⁺ and subsequently sustained by receptor-regulated Ca²⁺ influx. The selective .alpha.1A-AR agonist (R)-A-61603 was 141-fold more potent as an agonist than Phe. This potency ratio was consistent with the pharmacol. of the native .alpha.1A-ARs. Functional responses evoked by concns. of Phe of more than 0.3 .mu.M displayed fade, which could be explained by agonist-dependent depletion of Ca²⁺ stores. The antagonists tested did not conform to the predictions of the Schild equation for competitive antagonism as expected from the nonequil. nature of the response. The antagonist potency series WB 4101 .gtoreq. prazosin .mchgt. BMY 7378, however, was consistent with .alpha.1A-ARs. Antagonism exhibited by WB 4101 and prazosin was compatible with a model in which antagonists dissociate so slowly from the receptor that this is a major factor in their inhibition of the transient agonist-mediated response, leading to the appearance of insurmountable antagonism. A consequence of this phenomenon was that an inverse concn.-response relationship at high agonist concns. was abolished by low concns. of antagonists. Overall, the

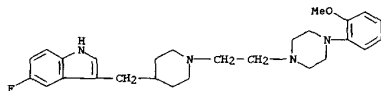
L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:345474 CAPLUS
 DOCUMENT NUMBER: 132:347587
 TITLE: Preparation of piperazinylalkylpiperidinyl(alkyl)indol es as serotonergic agents.
 INVENTOR(S): Kelly, Michael G.; Kang, Young H.
 PATENT ASSIGNEE(S): American Home Products Corporation, USA
 SOURCE: U.S., 6 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|------|----------|-------------------|------------|
| US 6066637 | A | 20000523 | US 1999-298202 | 19990423 |
| PRIORITY APPL. INFO.: | | | US 1998-100433P | P 19980429 |
| OTHER SOURCE(S): | | | MARPAT 132:347587 | |

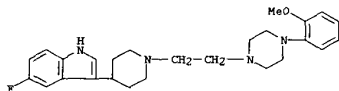


AB Title compds. {1: R₁ = H, OH, OR₂, F, Cl, Br, iodo; R₂ = alkyl; Q = (CH₂)_m; Q₁ = (CH₂)_n; n = 0-2; X = CH, CH₂; m = 2-4; Y = N, CH₂; Ar = (substituted) aryl, heteroaryl}, were prepd. Thus, 4-(5-fluoro-1H-indol-3-ylmethyl)piperidine, 1-(2-chloroethyl)-4-(2-methoxyphenyl)piperazine, and K2CO₃ were refluxed 5 h in MeCN to give 5-fluoro-3-[1-[2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl]piperidin-4-ylmethyl]-1H-indole. I displaced [3H]-paroxetine from serotonin transporters with K_i = 1.2-19 nM.
 IT 247911-01-9P 247911-02-0P 247911-03-3P
 247911-06-4P 247911-07-5P 247911-08-6P
 247911-09-7P 247911-12-2P 247911-14-4P
 247911-15-5P 247911-16-6P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological

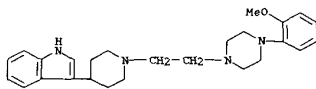
L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of piperazinyalkylpiperidinyl(alkyl)indoles as
 serotonergic
 agents)
 RN 247911-01-9 CAPLUS
 CN 1H-Indole,
 5-fluoro-3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-
 piperidinyl]methyl]- (9CI) (CA INDEX NAME)



RN 247911-02-0 CAPLUS
 CN 1H-Indole,
 5-fluoro-3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-
 piperidinyl]- (9CI) (CA INDEX NAME)

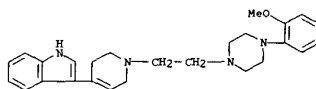


RN 247911-05-3 CAPLUS
 CN 1H-Indole, 3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-
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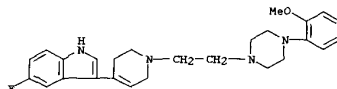


RN 247911-06-4 CAPLUS
 CN 1H-Indole, 3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4-pyridinyl]- (9CI) (CA INDEX NAME)

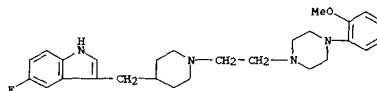
L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 247911-07-5 CAPLUS
 CN 1H-Indole, 5-fluoro-3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4-pyridinyl]- (9CI) (CA INDEX NAME)



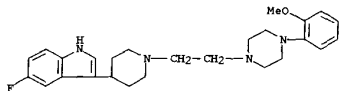
RN 247911-08-6 CAPLUS
 CN 1H-Indole,
 5-fluoro-3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-
 piperidinyl]methyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

RN 247911-09-7 CAPLUS
 CN 1H-Indole,
 5-fluoro-3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-
 piperidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

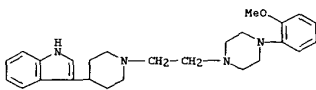


● 2 HCl

RN 247911-12-2 CAPLUS
 CN 1H-Indole, 3-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-
 piperidinyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

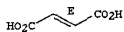
CRN 247911-05-3
 CMF C26 H34 N4 O



CM 2

CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.

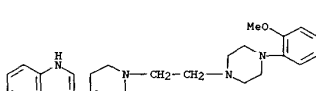


RN 247911-14-4 CAPLUS
 CN 1H-Indole, 3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4-pyridinyl]-, (2E)-2-butenedioate (2:1) (9CI)
 (CA INDEX NAME)

CM 1

CRN 247911-06-4
 CMF C26 H32 N4 O

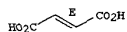
L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

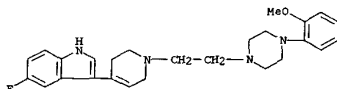
Double bond geometry as shown.



RN 247911-15-5 CAPLUS
 CN 1H-Indole, 5-fluoro-3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4-pyridinyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA
 INDEX NAME)

CM 1

CRN 247911-07-5
 CMF C26 H31 F N4 O



CM 2

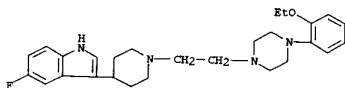
CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.



L14 ANSWER 35 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

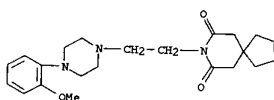
RN 247911-16-6 CAPLUS
CN 1H-Indole,
3-[1-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-
5-fluoro- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE
FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 36 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:345446 CAPLUS
DOCUMENT NUMBER: 133:99703
TITLE: Cloning of rabbit .alpha.1b-adrenoceptor and pharmacological comparison of .alpha.1a-, .alpha.1b- and .alpha.1d-adrenoceptors in rabbit
AUTHOR(S): Piao, H.; Taniguchi, T.; Nakamura, S.; Zhu, J.; Suzuki, F.; Mikami, D.; Muramatsu, I.
CORPORATE SOURCE: School of Medicine, Department of Pharmacology, Fukui Medical University, Matsuoka, Fukui, 910-1193, Japan
SOURCE: European Journal of Pharmacology (2000), 396(1), 9-17
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have isolated a cDNA clone of the rabbit .alpha.1b-adrenoceptor which has an open reading frame of 1557 nucleotides encoding a protein of 518 amino acids. The sequence shows higher identity to those of hamster, human, and rat .alpha.1b-adrenoceptors than to those of rabbit .alpha.1a- and .alpha.1d-adrenoceptors. The pharmacol. binding properties of this clone expressed in Cos-7 cells showed a characteristic profile as .alpha.1b-adrenoceptor; high affinity for prazosin (pKi=10.3), relatively high affinity for tamulosin (9.5) and low affinity for KMD 3213 (8.5), WB 4101 (8.7), and BMY 7378 (7.3). We have compared the levels of mRNA expression of three .alpha.1-adrenoceptor subtypes in rabbit tissues using the competitive reverse transcription/polymerase chain reaction (RT/PCR) assay. In most rabbit tissues except heart, .alpha.1a-adrenoceptor mRNA was expressed 10 folds more than the other two subtypes. However, binding expts. with [3H]prazosin and [3H]KMD 3213 in rabbit tissues revealed a poor relationship between binding d. and mRNA level. Esp., .alpha.1b binding sites were exclusively predominant in spleen, whereas the .alpha.1b subtype was minor at the mRNA level. These results indicate a high identity of structural and pharmacol. profiles of three distinct .alpha.1-adrenoceptor subtypes between rabbit and other species, but there are species differences in their distribution.
IT 21102-95-4, BMY 7378
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(rabbit .alpha.1b-adrenoceptor sequence and expression and pharmacol.

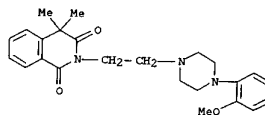
L14 ANSWER 36 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
comparison with other .alpha.1-adrenoceptor subtypes)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



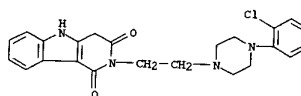
● 2 HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE
FOR THIS
FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 37 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:343282 CAPLUS
DOCUMENT NUMBER: 133:159627
TITLE: The ad hoc supermolecule approach to receptor ligand design
AUTHOR(S): De Benedetti, P. G.; Fanelli, F.; Menziani, M. C.; Cocchi, M.
CORPORATE SOURCE: Dipartimento di Chimica, Università di Modena e Reggio Emilia, Modena, 41100, Italy
SOURCE: THEOCHEM (2000), 503(1-2), 1-16
CODEN: THEODJ; ISSN: 0166-1280
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Among the ligand design methods based on the theor. QSAR paradigm, the simple ad hoc supermol. approach is presented and applied to a highly non-congeneric set of .alpha.1-adrenergic receptor antagonists. The performance of the approach is satisfactory and highlights its (semi)quant. ligand design potentiality.
IT 67339-62-2 288073-22-3
RL: RAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(ad hoc supermol. approach to receptor ligand design)
RN 67339-62-2 CAPLUS
CN 1,3-(2H,4H)-isoquinolinedione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



RN 288073-22-3 CAPLUS
CN 1H-Pyrido[4,3-b]indole-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,5-dihydro- (9CI) (CA INDEX NAME)



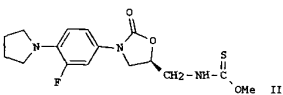
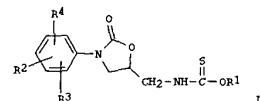
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR
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L14 ANSWER 37 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:335397 CAPLUS
DOCUMENT NUMBER: 132:334453
TITLE: Preparation of oxazolidinylmethylthiocarbamic acid
derivatives as antibacterial agents
INVENTOR(S): Kado, Noriyuki; Tokuyama, Ryukou; Tsubouchi,
Masatoshi; Tomita, Yayoi
PATENT ASSIGNEE(S): Hokuriku Seiyaku Co., Ltd., Japan
SOURCE: PCT Int. Appl., 137 pp.
CODEN: FIKXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

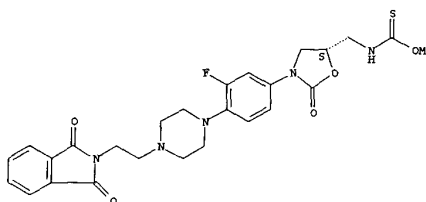
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|---|----------|-----------------|------------|
| WO 2000027830 | A1 | 20000518 | WO 1999-JP6260 | 19991110 |
| W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, | | | |
| CU, | CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, | | | |
| IL, | IN, IS, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, | | | |
| MG, | MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, | | | |
| SL, | TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, | | | |
| BY, | KG, KZ, MD, RU, TJ, TM | | | |
| DE, | HW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, | | | |
| CF, | DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, RF, BJ, | | | |
| | CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| JP 2000204084 | A2 | 20000725 | JP 1999-273230 | 19990927 |
| EP 1130016 | A1 | 20010905 | EP 1999-971804 | 19991110 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, | | | |
| PT, | IE, SI, LT, LV, FI, RO | | | |
| PRIORITY APPLN. INFO.: | | | JP 1998-320137 | A 19981111 |
| | | | JP 1999-273230 | A 19990927 |
| | | | WO 1999-JP6260 | W 19991110 |
| OTHER SOURCE(S): | MARPAT 132:334453 | | | |
| GI | | | | |

L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB The title compds. I [R1 is optionally substituted alkyl or optionally substituted cycloalkyl; and R2, R3 and R4 are each independently hydrogen, halogeno, optionally substituted alkyl, optionally substituted alkoxy, optionally substituted amino, optionally substituted alkanoyl, optionally substituted cycloalkyloxy contg. a heteroatom as the ring-constituting atom, or an optionally substituted satd. heterocyclic group, or alternatively any two of R2, R3 and R4 together with the benzene ring may form an optionally substituted fused hydrocarbon ring] are prepd. The title compd. II in vitro showed IC50 of 0.39 .mu.g/mL against *S. aureus*, vs. IC50 of 3.13 .mu.g/mL for linezolid.
IT 268208-40-8P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of oxazolidinylmethylthiocarbamic acid derivs. as antibacterial agents)
RN 268208-40-8 CAPLUS
CN Carbamothioic acid, [(5S)-3-[4-[2-(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)ethyl]-1-piperazinyl]-3-fluorophenyl]-2-oxo-5-oxazolidinylmethyl]-, O-methyl ester (9CI) (CA INDEX NAME)
Absolute stereochemistry. Rotation (-).

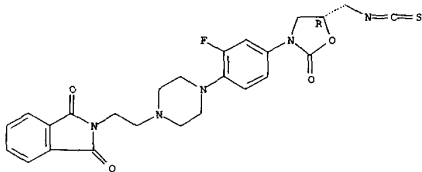
L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



IT 268208-92-0P 268209-56-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of oxazolidinylmethylthiocarbamic acid derivs. as antibacterial agents)
RN 268208-92-0 CAPLUS
CN 1H-isoindole-1,3(2H)-dione, 2-[2-[4-[4-[(5R)-5-(azidomethyl)-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)
Absolute stereochemistry. Rotation (-).

RN 268209-56-9 CAPLUS
CN 1H-isoindole-1,3(2H)-dione, 2-[2-[4-[2-fluoro-4-[(5R)-5-(isothiocyanatomethyl)-2-oxo-3-oxazolidinyl]phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)
Absolute stereochemistry. Rotation (-).

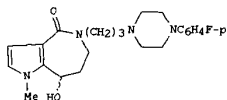
L14 ANSWER 38 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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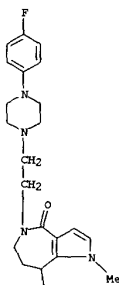
L14 ANSWER 39 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2000:311250 CAPLUS
DOCUMENT NUMBER: 133:104983
TITLE: Synthesis and serotonin 2 (5-HT₂) receptor
antagonist
activity of 5-aminoalkyl-substituted
pyrrolo[3,2-c]azepines and related compounds
AUTHOR(S): Mizuno, Akira; Ogata, Atsuo; Kamei, Tomoe;
Shibata, Makoto; Shimamoto, Tetsuo; Hayashi, Yasuhiro;
Nakanishi, Kyoko; Takiguchi, Chikako; Oka, Naomi;
Inomata, Norio
CORPORATE SOURCE: Suntory Institute for Biomedical Research, Osaka,
618-8503, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (2000), 48 (5),
623-635
CODEN: CPBTAL; ISSN: 0009-2363
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:104983
GI



AB A series of 5-aminoalkylpyrrolo[3,2-c]azepine derivs. was synthesized
and their serotonin 2 (5-HT₂) receptor antagonist and antiplatelet
aggregation activities were evaluated. 5-HT₂ receptor antagonist activity was
largely detd. by the nature of the substituent at the 8-position as well as
the aminoalkyl group at the 5-position of the pyrrolo[3,2-c]azepine ring.
Compd. 1 was recognized as having potent 5-HT₂ receptor antagonist
activity with weak .alpha.1 adrenoreceptor blocking activity and no
significant D2 receptor binding affinity. (+,+-)-1 was resolved
directly via diastereomeric salt formation and each enantiomer was evaluated.
The 5-HT₂ receptor antagonist activity of 1 was found to reside primarily
in (-)-1 (.alpha.-OH) (which was about 14-fold more potent than (+)-1
(.beta.-OH) in isolated guinea pig arteries). Consequently, (S)-(-)-1
(SUN C5174) displayed the overall best profile with potent 5-HT₂
receptor antagonist activity (pA₂=8.98+/-0.06) and high selectivity vs. other

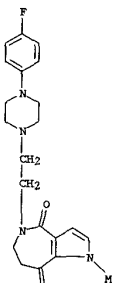
L14 ANSWER 39 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
receptors. SUN C5174 showed a marked inhibitory effect on the
platelet aggregation induced by serotonin in combination with collagen and
ADP in canine or human platelet-rich plasma (IC₅₀=6.5 to 16 nM). SUN C5174
significantly inhibited the mortality rate in mouse acute pulmonary
thromboembolic death induced by collagen and serotonin at oral
doses of 0.3 mg/kg or higher. SUN C5174 is currently undergoing clin.
evaluation.
IT 191592-08-2#
RL: RAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation);
BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and serotonin 2 (5-HT₂) receptor antagonist activity of
5-aminoalkyl-substituted pyrrolo[3,2-c]azepines and related
compds.)
RN 191592-08-2 CAPLUS
CN Pyrrolo[3,2-c]azepin-4(1H)-one, 5-[2-[4-(4-fluorophenyl)-1-
piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-hydroxy-1-methyl- (9CI) (CA
INDEX NAME)



PAGE 1-A

L14 ANSWER 39 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

IT 191591-85-2#
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(prepn. and serotonin 2 (5-HT₂) receptor antagonist activity of
5-aminoalkyl-substituted pyrrolo[3,2-c]azepines and related
compds.)
RN 191591-85-2 CAPLUS
CN Pyrrolo[3,2-c]azepine-4,8(1H,5H)-dione, 5-[2-[4-(4-fluorophenyl)-1-
piperazinyl]ethyl]-6,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



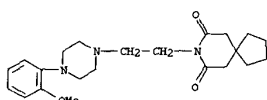
PAGE 1-A



PAGE 2-A

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR
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L14 ANSWER 40 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
unique in C-terminal sequence and in tissue distribution. They show similar pharmacol. profiles in binding studies but
.alpha.1a-OCU.3-AR had the highest potency of noradrenaline in functional studies in spite of the lowest receptor d. These findings suggest that the structure of C-terminus of .alpha.1a-ARs may give the characteristic functional profile.
IT 21102-95-4, BMY 7378
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(.alpha.1a-adrenoceptor splice isoform sequence and functional expression and pharmacol. characterization in rabbit)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

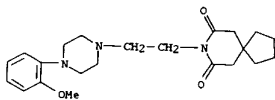


● 2 HCl

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 40 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:309881 CAPLUS
DOCUMENT NUMBER: 133:69131
TITLE: Splice isoforms of .alpha.1a-adrenoceptor in rabbit
AUTHOR(S): Suzuki, Fumiko; Taniguchi, Takanobu; Takauji, Rumiko
CORPORATE SOURCE: Murata, Satoshi; Muramatsu, Ikunobu
Department of Pharmacology, School of Medicine, Fukui
Medical University, Fukui, 910-1193, Japan
SOURCE: British Journal of Pharmacology (2000), 129(8), 1569-1576
CODEN: BJPCRM; ISSN: 0007-1188
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two splice isoforms of rabbit .alpha.1a-adrenergic receptor (AR), (named .alpha.1a-OCU.2-AR and .alpha.1a-OCU.3-AR) have been isolated from the liver cDNA library in addn. to the previously reported isoform (.alpha.1a-OCU.1-AR). Although they have the identical splice position with human .alpha.1a-AR isoforms, the C-terminal sequences are distinct from those of human isoforms. Among these rabbit .alpha.1a-AR isoforms, there are no significant differences in pharmacol. properties: high affinity for prazosin, WB 4101, KMD-3213 and YM 617 and low affinity for BMY 7378, using COS-7 cells expressing each isoform by radioligand binding assay. Competitive reverse transcription-polymerase chain reaction (RT-PCR) anal. revealed that mRNA of .alpha.1a-ARs was expressed in liver, thoracic aorta, brain stem and thalamus of rabbit. The splice isoforms exhibited a distinct distribution pattern in rabbit: .alpha.1a-OCU.1-AR was expressed most abundantly in those tissues. CHO clones, stably expressing each isoforms with receptor d. 740 fmol mg⁻¹ protein in .alpha.1a-OCU.1-AR, 1200 fmol mg⁻¹ in .alpha.1a-OCU.2-AR and 570 fmol mg⁻¹ in .alpha.1a-OCU.3-AR, resp., showed a noradrenaline-induced increase in inositol trisphosphate which was suppressed by prazosin. Noradrenaline elicited a concn.-dependent increase in extracellular acidification rate (EAR) in the CHO clones with pEC50 values of 6.19 for .alpha.1a-OCU.1-AR, 6.49 for .alpha.1a-OCU.2-AR and 6.58 for .alpha.1a-OCU.3-AR, resp. Noradrenaline caused a concn.-dependent increase in intracellular Ca²⁺ concn. ([Ca²⁺]_i) in the CHO clones with pEC50 values of 6.14 for .alpha.1a-OCU.1-AR, 7.25 for .alpha.1a-OCU.2-AR and 7.70 for .alpha.1a-OCU.3-AR, resp. In conclusion, the present study shows the occurrence of three splice isoforms of rabbit .alpha.1a-AR, which are

L14 ANSWER 41 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:273553 CAPLUS
DOCUMENT NUMBER: 133:13034
TITLE: .alpha.1-Adrenoceptor subtypes mediating contractions of the rat mesenteric artery
AUTHOR(S): Russain, M. B.; Marshall, I.
CORPORATE SOURCE: Department of Pharmacology, University College London, London, UK
SOURCE: European Journal of Pharmacology (2000), 395(1), 69-76
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The .alpha.1-adrenoceptor subtype(s) mediating contractions of the rat mesenteric artery were investigated using the agonists methoxamine, cirazoline, P 7480 and subtype-selective antagonists including BMY 7378. The pA₂ or apparent pK_B values of antagonists against methoxamine contractions correlated best with its pK_i values at the cloned .alpha.1b-(0.88), with cirazoline, antagonists affinities correlated equally well with those at .alpha.1a-(0.79) or the .alpha.1b-(0.81) while with P 7480 antagonist affinities correlated best with the .alpha.1d-adrenoceptor subtype (0.94). The low affinity est. for 5-methylurapidil (7.5) against the .alpha.1a-selective cirazoline suggests an .alpha.1A-subtype mediating contraction is unlikely. Shallow Schild plot slopes of subtype selective antagonists against all three agonists are consistent with heterogeneity of .alpha.1-adrenoceptors. P 7480 (putative .alpha.1D-adrenoceptor-selective) acts primarily at this subtype and at another which is more likely to be an .alpha.1B- than an .alpha.1A-adrenoceptor. The results with both agonists and antagonists are consistent with contractions of the rat mesenteric artery being mediated via the .alpha.1D- and possibly .alpha.1B-adrenoceptor.
IT 21102-95-4, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.1-adrenoceptor subtypes mediating contractions of rat mesenteric artery and pharmacol. characterization thereof)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

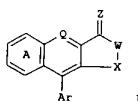


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REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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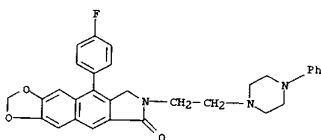
L14 ANSWER 42 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:218572 CAPLUS
DOCUMENT NUMBER: 132:260701
TITLE: Tricyclic compounds, their preparation, and cyclic GMP phosphodiesterase inhibitors
INVENTOR(S): Teuburai, Shogo; Doi, Takayuki; Tarui, Naoki
PATENT ASSIGNEE(S): Takeda Chemical Industries, Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 71 pp.
CODEN: JKKXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|-------------------|-----------------|----------|
| JP 2000095759 | A2 | 20000404 | JP 1999-204103 | 19990719 |
| PRIORITY APPLN. INFO.: | | | JP 1998-204963 | 19980721 |
| OTHER SOURCE(S): | | MARPAT 132:260701 | | |



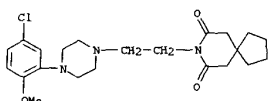
AB Title inhibitors contain tricyclic compds. I (ring A = (substituted) benzene ring; W = (substituted) NH; Q = CR, N; R = H, (substituted) alkyl, (substituted) alkoxy; X = (substituted) C1-2 alkylene; Z = H2, O; Ar = (substituted) arom. hydrocarbyl, (substituted) arom. heterocyclyl) or their salts. (6-Bromo-1,3-benzodioxol-5-yl)methanol (4.0 g) was treated with BuLi followed by 2.3 g 4-FC6H4CN in THF/hexane at room temp. for 2 h and treated with 3.5 g maleimide and p-MeC6H4SO3H in PhMe under reflux for 15 h to give 5.6 g I (ring A = 1,3-benzodioxole, W = NH, Q = CH, X = CO, Z = O, Ar = C6H4F-p). I (ring A = 1,3-benzodioxole, W = 4-pyridylmethylimino, Q = CH, X = CH2, Z = O, Ar = C6H4F-p) in vitro inhibited recombinant human phosphodiesterase with IC50 of 8.3 nM. Formulation examples are given.
IT 263018-67-3p
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of tricyclic compds. as cyclic GMP phosphodiesterase

L14 ANSWER 42 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
inhibitors)
RN 263018-67-3 CAPLUS
CN 6H-1,3-Benzodioxolo[5,6-f]isoindol-6-one,
9-(4-fluorophenyl)-7,8-dihydro-7-[2-(4-phenyl-1-piperazinyl)ethyl]- (9C1) (CA INDEX NAME)



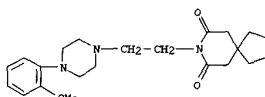
L14 ANSWER 43 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:171777 CAPLUS
DOCUMENT NUMBER: 132:303466
TITLE: Effects of intracavernous administration of selective antagonists of .alpha.1-adrenoceptor subtypes on erection in anesthetized rats and dogs
AUTHOR(S): Sironi, Giorgio; Colombo, Davide; Poggesi, Elena; Leonardi, Amedeo; Testa, Rodolfo; Rampin, Olivier; Bernabe, Jacques; Giuliano, Francois
CORPORATE SOURCE: Pharmaceutical R and D Division, Milan, Italy
Therapeutics
(2000), 292(3), 974-981
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The proerectile properties of three novel .alpha.1-adrenoceptor (.alpha.1-ADR) antagonists with different profiles of selectivity for the .alpha.1-ADR subtypes have been evaluated in anesthetized rats and dogs on intracavernous (IC) injection, in comparison with prazosin and phentolamine. In rats, the tested compds. decreased blood pressure (BP) and increased IC pressure (ICP), as well as the ratio ICP/BP. Rec 15/2841 (.alpha.1a- plus .alpha.1L-ADR-selective antagonist) and Rec 15/2615 (.alpha.1b-ADR selective) were the most potent compds. The ICP/BP ratios calcd. after injection of Rec 15/3039 (.alpha.1d-ADR selective) were not markedly different from those obsd. after vehicle injection. Prazosin and phentolamine proved poorly active, their main effect being hypotension. Approx. ED25 values (dose of compd. in micrograms inducing 25% increase of ICP/BP ratio) were Rec 15/2615 (22 .mu.g/kg) > Rec 15/2841 (29 .mu.g/kg) > prazosin (136 .mu.g/kg) > phentolamine (1298 .mu.g/kg) > Rec 15/3039 (9600 .mu.g/kg). Submaximal stimulation of the cavernous nerve elicited an ICP rise whose amplitude was not altered by Rec compds. In contrast, prazosin and phentolamine decreased this ICP rise. All compds. but 15/3039 induced significant increase of the ICP/BP ratio in dogs. Rec 15/2615 proved to be the most interesting compd., inducing significant increases of ICP/BP at doses practically devoid of effects on BP. The rank order of potency in dog in increasing the ICP/BP ratio was similar to that obsd. in rats. Only at the highest doses tested, all compds., except Rec 15/3039, decreased the ICP rise elicited by submaximal stimulation of

L14 ANSWER 43 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
the cavernous nerve. Our data demonstrate that the .alpha.1b- and .alpha.1L-ADR subtypes are functionally relevant for the erectile function in these models, and that .alpha.1b- and/or .alpha.1L-ADR subtypes selective antagonists could represent a real advantage in erectile dysfunction therapy.
IT 252240-56-5, REC 15/3039
RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (effects of intracavernous administration of selective antagonists of .alpha.1-adrenoceptor subtypes on erection in anesthetized rats and dogs)
RN 252240-56-5 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(5-chloro-2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



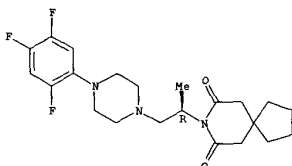
REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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L14 ANSWER 44 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:125868 CAPLUS
DOCUMENT NUMBER: 132:245855
TITLE: Ligand design for .alpha.1-adrenoceptor subtype selective antagonists
AUTHOR(S): Bremner, John B.; Coban, Burak; Griffith, Renate; Groenewoud, Karina M.; Yates, Brian F.
CORPORATE SOURCE: Department of Chemistry, University of Wollongong, Wollongong, 2522, Australia
SOURCE: Biorganic & Medicinal Chemistry (2000), 8(1), 201-214
CODEN: BMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB .alpha.1-Adrenoceptors have three subtypes and drugs interacting selectively with these subtypes could be useful in the treatment of a variety of diseases. In order to gain an insight into the structural principles governing subtype selectivity, ligand based drug design (pharmacophore development) methods have been used to design a novel 1,2,3-thiadiazole ring D analog of the aporphine system. Synthesis and testing of this compd. as a ligand on cloned and expressed human .alpha.1-adrenoceptors is described. Low binding affinity was found, possibly due to an unfavorable electrostatic potential distribution. Pharmacophore models for antagonists at the three adrenoceptor sites (.alpha.1A, .alpha.1B, .alpha.1D) were generated from a no. of different training sets and their value for the design of new selective antagonists discussed. The first preliminary antagonist pharmacophore model for the .alpha.1D adrenoceptor subtype is also reported.
IT 21102-95-4, BMY-7378 255893-38-0, SNAP 8719
RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (ligand design for .alpha.1-adrenoceptor subtype selective antagonists)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L14 ANSWER 44 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 255893-38-0 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-(4-(2,4,5-trifluorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)
Absolute stereochemistry.

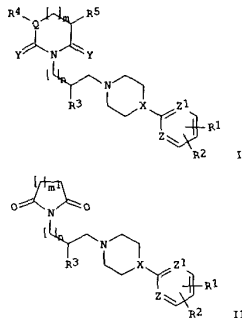


REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 45 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:84765 CAPLUS
DOCUMENT NUMBER: 132:122634
TITLE: Preparation of arylpiperazines as uro-selective .alpha.1-adrenoceptor blockers
INVENTOR(S): Anand, Nitya; Sinha, Neelima; Jain, Sanjay; Mehta, Anita; Saxena, Anil Kumar; Gupta, Jang Bahadur
PATENT ASSIGNER(S): Ranbaxy Laboratories Limited, India
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

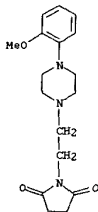
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|---|-----------------|----------|
| WO 2000005205 | A1 | 20000203 | WO 1999-1B140 | 19990126 |
| DE, | W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, | | |
| JP, | | DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, | | |
| MN, | | KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, | | |
| TM, | | MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, | | |
| RU, | | TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, BG, KZ, MD, | | |
| | | TJ, TM | | |
| ES, | RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, | | |
| CI, | | FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, | | |
| | | CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | |
| US 6083950 | A | 20000704 | US 1998-120265 | 19980721 |
| AU 9919797 | A1 | 20000214 | AU 1999-19797 | 19990126 |
| WO 2000005205 | A1 | 20000203 | WO 1999-1B1296 | 19990716 |
| CZ, | W: | AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, | | |
| IS, | | DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, | | |
| MK, | | JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, | | |
| TJ, | | MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, | | |
| KZ, | | TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, | | |
| | | MD, RU, TJ, TM | | |
| DK, | RW: | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, | | |
| CG, | | ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, | | |
| | | CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | |
| AU 9946410 | A1 | 20000214 | AU 1999-46410 | 19990716 |
| BR 9912318 | A | 20010502 | BR 1999-12318 | 19990716 |
| EP 1097134 | A1 | 20010509 | EP 1999-929633 | 19990716 |
| PT, | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, | | |

L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 IE, SI, LT, LV, FI, RO
 JP 2002521362 T2 20020716 JP 2000-561162 19990716
 PRIORITY APPLN. INFO.: US 1998-120265 A 19990721
 WO 1999-18140 W 19990126
 IN 1997-DE3260 A 19971113
 IN 1997-DE3261 A 19971113
 IB 1999-189900140A 19990126
 WO 1999-181296 W 19990716
 OTHER SOURCE(S): MARPAT 132:107963
 GI



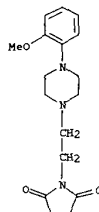
AB The title compds. [I: Y = O, S; Q, X, Z, and Z1 = CH, N; m = 0-3, n = 0-4; R1, R2 = H, F, Cl, etc.; R3 = H, R6, OH, OR6; R6 = alkyl; R4, R5 = H, alkyl, (un)substituted Ph, etc.] and more preferred compds. II [m1 = 1-4] which have been found to exhibit selective .alpha.1A adrenergic activity, were prepd. Thus, reacting 2,5-dioxopyrrolidine with 1-[4-(4-fluorophenyl)piperazin-1-yl]-3-chloropropane in the presence of K2CO3 and Bu4NBr in Me2CO afforded 65% II [m1 = 1; n = 1; X = N; Z = Z1 = CH; R1 = 4-F; R2 = R3 = H]. Biol. data for compds. II were given. The compds. I

L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

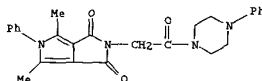
L14 ANSWER 46 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 and II are useful for treatment of disease conditions, such as peripheral vascular disease, congestive heart failure, hypertension and esp. benign prostatic hypertrophy.
 IT 255861-61-1P 255861-79-1P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) [prepn. of arylpiperazines as uro-selective .alpha.1-adrenoceptor blockers]
 RN 255861-61-1 CAPLUS
 CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

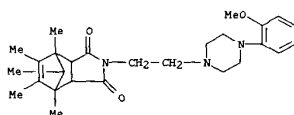
RN 255861-79-1 CAPLUS
 CN 2,5-Pyrrolidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 47 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:74842 CAPLUS
 DOCUMENT NUMBER: 132:22466
 TITLE: Synthesis of some N-substituted 3,4-pyrroledicarboximides as potential CNS depressive agents
 AUTHOR(S): Malinka, W.; Sieklucka-Dziuba, M.; Rajtar, G.; Rejdak, R.; Rejdak, K.; Kleinrok, Z.
 CORPORATE SOURCE: Department of Chemistry of Drugs, Wroclaw Medical University, Lublin, Pol.
 SOURCE: Pharmazie (2000), 55(1), 9-16
 CODEN: PHARAT; ISSN: 0031-7144
 PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Several novel N-substituted 3,4-pyrroledicarboximides were prepd. and eleven representatives were examd. in a series of in vivo CNS tests.
 A few of these compds. displayed a similar profile of biol. selectivity to that of 3,4-pyrroledicarboximides described previously; their structure-activity relationships are discussed.
 IT 261164-81-2P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) [prepn. of pyrroledicarboximides as potential CNS depressive agents]
 RN 261164-81-2 CAPLUS
 CN Piperazine, 1-[(3,5-dihydro-4,6-dimethyl-1,3-dioxo-5-phenylpyrrolo[3,4-c]pyrrol-2(1H)-yl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 48 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:74841 CAPLUS
 DOCUMENT NUMBER: 132:222411
 TITLE: Synthesis of new derivatives of 1,2,3,4,7-pentamethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboximide with an expected anxiolytic activity
 AUTHOR(S): Kossakowski, J.; Kusmierczyk, J.
 CORPORATE SOURCE: Department of Medical Chemistry, Medical University of
 SOURCE: Warsaw, Pol.
 Pharmazie (2000), 55(1), 5-8
 CODEN: PHARAT; ISSN: 0031-7144
 PUBLISHER: Govi-Verlag Pharmazeutischer Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The prepn. of a no. of derivs. of 1,2,3,4,7-pentamethylbicyclo[2.2.1]hept-2-ene-5,6-dicarboximide with potential anxiolytic activity has been described. The aim of our study was to obtain new analogs of tandospirone, that is derivs. of cyclic imides.
 IT 261160-88-7P 261160-90-1P 261160-92-3P
 RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (prepn. and anxiolytic activity of pentamethylbicycloheptenedicarboximide)
 RN 261160-88-7 CAPLUS
 CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,5,6,7,8-pentamethyl-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

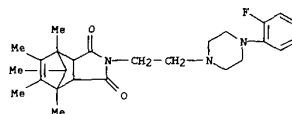
RN 261160-90-1 CAPLUS
 CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[2-[4-(2-fluorophenyl)-1-piperazinyl]ethyl]-3a,4,7,7a-tetrahydro-4,5,6,7,8-pentamethyl-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:68449 CAPLUS
 DOCUMENT NUMBER: 132:107961
 TITLE: Preparation of 8-[2-piperazino(or piperidino)ethyl]-8-azaspiro[4.5]decane-7,9-diones as specific ligands for the human .alpha.1d adrenergic receptor
 INVENTOR(S): Konkel, Michael; Wetzel, John M.; Noble, Stewart; Gluchowski, Charles; Craig, Douglas A.
 PATENT ASSIGNER(S): Synaptic Pharmaceutical Corporation, USA
 SOURCE: PCT Int. Appl., 97 pp.
 CODEN: PIXMD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 2000004012 | A1 | 20000127 | WO 1999-US16101 | 19990716 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 9952146 | A1 | 20000207 | AU 1999-52146 | 19990716 |
| EP 1100794 | A1 | 20010523 | EP 1999-937273 | 19990716 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002520408 | T2 | 20020709 | JP 2000-560118 | 19990716 |
| US 2002028760 | A1 | 20020307 | US 2001-764710 | 20010117 |
| PRIORITY APPLN. INFO.: | | | US 1998-118323 | A2 19980717 |
| | | | WO 1999-US16101 | W 19990716 |

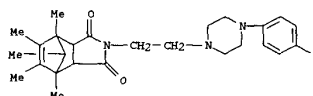
OTHER SOURCE(S): MARPAT 132:107961
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L14 ANSWER 48 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



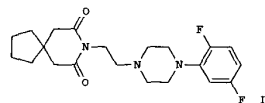
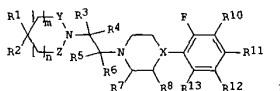
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RN 261160-92-3 CAPLUS
 CN 4,7-Methano-1H-isoindole-1,3(2H)-dione, 2-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-3a,4,7,7a-tetrahydro-4,5,6,7,8-pentamethyl-, dihydrochloride (9CI) (CA INDEX NAME)



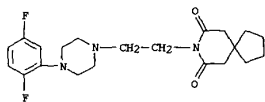
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L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

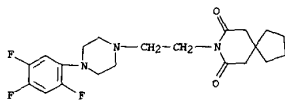


AB The title compds. [I; n = 0-2; m = 0-2; Y = CH2, CO, CS; Z = CH2, CO, CS; R1, R2 = H, alkyl, alkoxy, etc.; R3 = H, alkyl, alkenyl, etc.; R4 = H, Me; R5 = H, alkyl, alkenyl, etc.; R6 = H, alkyl, alkenyl, etc.; R7 = H, alkyl, alkenyl, etc.; R8 = H, Me; R10 = H, F; R11 = H, F, Cl, etc.; R12 = H, F, Cl, etc.; R13 = H, F; X = N, CH] which binds selectively to a human .alpha.1d adrenergic receptor, and are useful in treating hypertension, Raynaud's disease, and urinary incontinence, were prepd. and formulated.
 Thus, heating 1-(2,5-difluorophenyl)piperazine with 8-(2-chloroethyl)-8-azaspiro[4.5]decane (preps. were given) afforded II which showed pKi of 9.0 at .alpha.1d receptor.
 IT 255893-35-7P 255893-36-8P 255893-37-9P
 255893-38-0P 255893-39-1P 255893-40-4P
 255893-42-6P 255893-43-7P 255893-44-8P
 255893-45-9P 255893-46-0P 255893-48-2P
 255893-50-6P 255893-51-7P 255893-52-8P
 RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of 8-(2-piperazino(or piperidino)ethyl)-8-azaspiro[4.5]decane-7,9-diones as specific ligands for the human .alpha.1d adrenergic receptor)
 RN 255893-35-7 CAPLUS

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-difluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

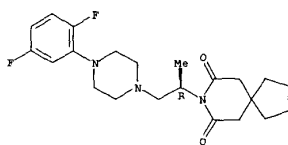


RN 255893-36-8 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 255893-37-9 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-2-[4-(2,5-difluorophenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)

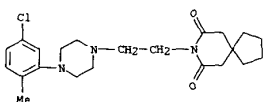
Absolute stereochemistry.



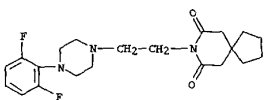
RN 255893-38-0 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

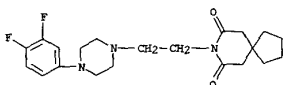
L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 255893-42-6 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 255893-43-7 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,6-difluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



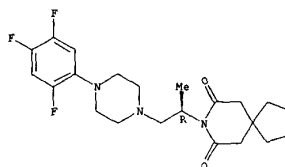
RN 255893-44-8 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3,4-difluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 255893-45-9 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-phenyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

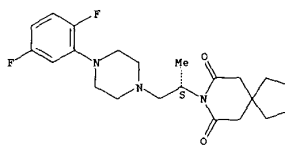
Absolute stereochemistry.

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



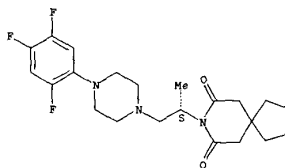
RN 255893-39-1 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1S)-2-[4-(2,5-difluorophenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

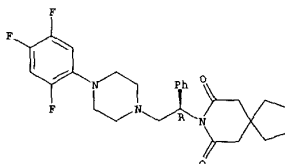


RN 255893-40-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1S)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

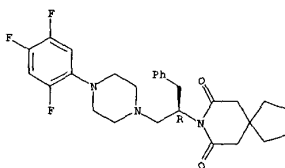


L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

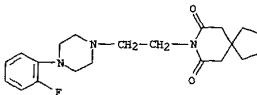


RN 255893-46-0 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[(1R)-1-(phenylmethyl)-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

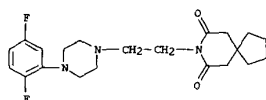


RN 255893-48-2 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



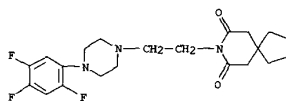
RN 255893-50-6 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2,5-difluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 255893-51-7 CAPLUS
CN 8-Azaspino[4.5]decane-7,9-dione, 8-[2-(4-(2,4,5-trifluorophenyl)-1-piperazinyl)ethyl]-, hydrochloride (5:6) (9CI) (CA INDEX NAME)

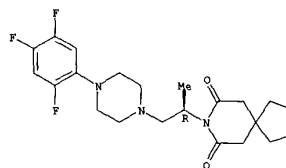


● 6/5 HCl

RN 255893-52-8 CAPLUS
CN 8-Azaspino[4.5]decane-7,9-dione, 8-[(1R)-1-methyl-2-[4-(2,4,5-trifluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.

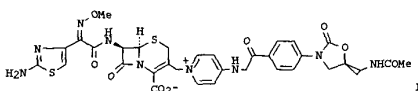
L14 ANSWER 49 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 50 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:26717 CAPLUS
DOCUMENT NUMBER: 132:207679
TITLE: Synthesis and in vitro antibacterial activity of quaternary ammonium cephalosporin derivatives bearing
AUTHOR(S): Chung, In Hwa; Kim, Choong Sup; Seo, Jae Hong; Chung, Bong Young
CORPORATE SOURCE: Biochemicals Research Center, Korea Institute of Science and Technology, Seoul, 130-650, S. Korea
SOURCE: Archives of Pharmacol Research (1999), 22(6), 579-584
PUBLISHER: Pharmaceutical Society of Korea
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



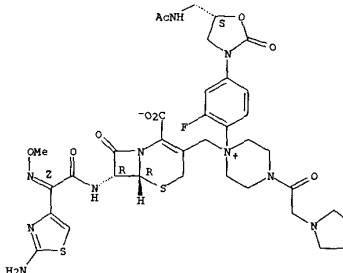
AB Several oxazolidinones having amine moiety were prepd. to form a quaternary ammonium salt with cephalosporin nucleus, and antibacterial activity of the quaternary ammonium cephalosporin derivs. (e.g., 1) bearing oxazolidinone moiety were examd. particularly with expectation of dual activity. However, the cephalosporin-oxazolidinone compds. revealed rather weaker antibacterial activity in vitro than their parent oxazolidinone and cephalosporin without showing any characteristic activity as expected.

IT 260262-92-89
RL: EAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (synthesis and antibacterial activity of quaternary ammonium oxazolidinonocephalosporin derivs.)

RN 260262-92-8 CAPLUS
CN Piperazinium, 1-[4-[(5S)-5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1-[[[(6R,7R)-7-[[[(2Z)-(2-amino-4-thiazolyl)methoxyimino]acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]-4-(1-pyrrolidinylacetyl)]-, inner salt (9CI) (CA INDEX NAME)

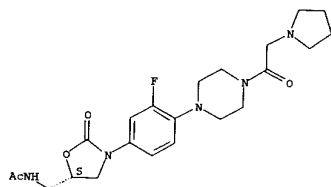
L14 ANSWER 50 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

Absolute stereochemistry.
Double bond geometry as shown.



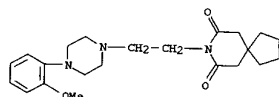
IT 260262-82-6
RL: RCI (Reactant); RACT (Reactant or reagent) (synthesis and antibacterial activity of quaternary ammonium oxazolidinonocephalosporin derivs.)
RN 260262-82-6 CAPLUS
CN Acetamide, N-[[[(5S)-3-[3-fluoro-4-[4-(1-pyrrolidinylacetyl)-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



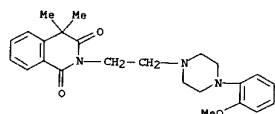
REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 51 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:9434 CAPLUS
 DOCUMENT NUMBER: 132:146156
 TITLE: Relevance of theoretical molecular descriptors in quantitative structure-activity relationship analysis
 of .alpha.1-adrenergic receptor antagonists
 AUTHOR(S): Menziani, M. C.; Montorsi, M.; De Benedetti, P. G.; Karelson, M.
 CORPORATE SOURCE: Department of Chemistry, University of Modena and Reggio Emilia, Modena, 41100, Italy
 SOURCE: Bioorganic & Medicinal Chemistry (1999), 7(11), 2437-2451
 CODEN: BMECEP; ISSN: 0968-0896
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A quant. structure-activity relationship (QSAR) study of a wide series of structurally diverse .alpha.1-adrenergic receptor antagonists was performed using the CODESSA (Comprehensive Descriptors for Structural and Statistical Anal.) technique. Theor. descriptors derived on a single structure and ad hoc defined size and shape descriptors were considered in the attempt of describing information relevant to receptor interaction.
 The relative effectiveness of these two classes of parameters in developing QSAR models for native (.alpha.1A and .alpha.1B) and cloned (.alpha.1a, .alpha.1b, and .alpha.1d) adrenergic receptor binding affinity, functional activity of vascular and lower urinary tract tissues, and in vitro and in vivo selectivity was evaluated.
 IT 21102-95-4, RMY 7378 67339-62-2, ARC 239
 99718-67-9
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (relevance of theor. mol. descriptors in QSAR anal. of .alpha.1-adrenergic receptor antagonists)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

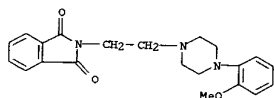


● 2 HCl

RN 67339-62-2 CAPLUS
 CN 1,3-(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



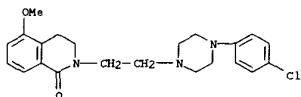
RN 99718-67-9 CAPLUS
 CN 1H-Isoindole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



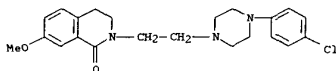
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 52 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:815373 CAPLUS
 DOCUMENT NUMBER: 132:165762
 TITLE: A Structure-Affinity Relationship Study on Derivatives of N-[2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl]-3-methoxybenzamide, a High-Affinity and Selective D4 Receptor Ligand
 AUTHOR(S): Perrone, Roberto; Berardi, Francesco; Colabufo, Nicola
 CORPORATE SOURCE: A.; Leopoldo, Marcello; Tortorella, Vincenzo
 SOURCE: Dipartimento Farmaco-Chimico, Università di Bari, Bari, 70126, Italy
 270-277
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB N-[2-[4-(4-Chlorophenyl)piperazin-1-yl]ethyl]-3-methoxybenzamide, a high-affinity and selective dopamine D4 receptor ligand, was chosen as a lead, and structural modifications were done on its amide bond and on its alkyl chain linking the benzamide moiety to the piperazine ring and by prep. some semirigid analogs. The binding profile at dopamine D4 and dopamine D2, serotonin 5-HT1A, and adrenergic .alpha.1 receptors of 16 new compds. was detd. From the results emerged that the modification of the amide bond and the elongation of the intermediate alkyl chain caused a decrease in dopamine D4 receptor affinity. All prep. semirigid analogs displayed D4 receptor affinity values in the same range of the opened counterparts.
 IT 258882-65-4P 258882-66-5P 258882-70-9P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. of deriva. of [(chlorophenyl)piperazinyl]ethyl]methoxybenzamide as selective D4 receptor ligand)
 RN 258882-65-4 CAPLUS
 CN 1(2H)-Isoquinolinone, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-3,4-dihydro-5-methoxy- (9CI) (CA INDEX NAME)

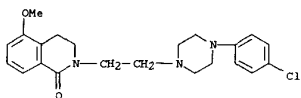
L14 ANSWER 52 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 258882-66-5 CAPLUS
CN 1 (2H)-isoquinolinone,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-3,4-
dihydro-7-methoxy-, (9CI) (CA INDEX NAME)



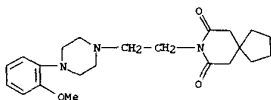
RN 258882-78-9 CAPLUS
CN 1 (2H)-isoquinolinone,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-3,4-
dihydro-5-methoxy-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 53 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(constitutive G12-dependent activation of adenylyl cyclase type
II by 5-HT1A receptor and inhibition by anxiolytic partial agonists)
RN 21102-95-4 CAPLUS
CN 8-Azasp[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

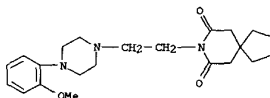


● 2 HCl

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 53 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:805403 CAPLUS
DOCUMENT NUMBER: 132:117709
TITLE: Constitutive G12-dependent activation of adenylyl
cyclase type II by the 5-HT1A receptor.
Inhibition by anxiolytic partial agonists
AUTHOR(S): Albert, Paul R.; Sajedi, Naghmeh; Lemonde, Sylvie;
Ghahremani, Mohammad H.
CORPORATE SOURCE: Neuroscience Research Institute, Departments of
Medicine and Cellular and Molecular Medicine,
University of Ottawa, Ottawa, ON, K1H 8M5, Can.
SOURCE: Journal of Biological Chemistry (1999), 274(50),
35469-35474
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular
Biology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 5-HT1A receptor is implicated in depression and anxiety. This
receptor couples to Gi proteins to inhibit adenylyl cyclase (AC)
activity but can stimulate AC in tissues (e.g., hippocampus) that express ACII.
The role of ACII in receptor-mediated stimulation of cAMP formation
was exand. in HEK-293 cells transfected with the 5-HT1A receptor, which
mediated inhibition of basal and Gs-induced cAMP formation in the
absence of ACII. In cells cotransfected with 5-HT1A receptor and ACII
plasmids, 5-HT1A agonists induced a 1.5-fold increase in cAMP level.
Cotransfection of 5-HT1A receptor, ACII, and G.alpha.i2, but not G.alpha.i1,
G.alpha.i3, or G.alpha.o, resulted in an agonist-independent 6-fold increase in
the basal cAMP level, suggesting that G12 preferentially coupled the
receptor to ACII. The 5-HT1B receptor also constitutively activated ACII.
Constitutive activity of the 5-HT1A receptor was blocked by pertussis
toxin and the G.beta.gamma. antagonist, .beta.CT, suggesting an
important role for G.beta.gamma.-mediated activation of ACII. The Thr 149
fwldw. Ala mutation in the second intracellular domain of the 5-HT1A receptor
disrupted G.beta.gamma.-selective activation of ACII. Spontaneous
5-HT1A receptor activity was partially attenuated by 5-HT1A receptor partial
agonists with anxiolytic activity (e.g., buspirone and flesinoxan)
but was not altered by full agonists or antagonists. Thus, anxiolytic
activity may involve inhibition of spontaneous 5-HT1A receptor activity.
IT 21102-95-4, EMY-7378
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); BIOL (Biological study)

L14 ANSWER 54 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:780562 CAPLUS
DOCUMENT NUMBER: 132:216950
TITLE: Interaction of clozapine and other antipsychotic
drugs with human .alpha.1-adrenergic receptor subtypes
AUTHOR(S): Brooks, Karen M.; Cai, Jidong; Sandrasagra,
Anthony;
CORPORATE SOURCE: Roehr, Joachim E.; Errazo, Rowena; Vargas, Hugo M.
General Pharmacology, Hoechst Marion Roussel,
Inc., Bridgewater, NJ, 08807-0800, USA
SOURCE: Proceedings of the Western Pharmacology Society
(1999), 42, 67-69
CODEN: WFPSA8; ISSN: 0083-8969
PUBLISHER: Western Pharmacology Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antipsychotic drugs bind to a variety of neurotransmitter receptors.
Blockage of brain .alpha.1-adrenergic receptors may contribute to the
clin. efficacy and low extrapyramidal side effects of atypical
antipsychotics. The authors evaluated clozapine and other
antipsychotic drugs for interaction with human .alpha.1-adrenergic receptor
subtypes. The atypical antipsychotic drug clozapine demonstrated high affinity
for each of the recombinant human .alpha.1-adrenergic receptors.
IT 21102-95-4, EMY 7378
RL: ADV (Adverse effect, including toxicity); BAC (Biological
activity or effector, except adverse); BFR (Biological process); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological study);
PROC (Process); USES (Uses)
(interaction of clozapine and other antipsychotic drugs with human
.alpha.1-adrenergic receptor subtypes)
RN 21102-95-4 CAPLUS
CN 8-Azasp[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

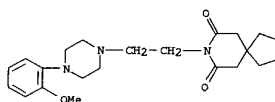


● 2 HCl

REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR
THIS

L14 ANSWER 54 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 55 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:750546 CAPLUS
DOCUMENT NUMBER: 132:216777
TITLE: Segmental differences in rat aorta contraction induced
by phenylephrine in aortic rings
AUTHOR(S): Arzun-Bojalil, Juan/ Escalante-Acosta, Bruno/ Ceballos-Reyes, Guillermo/ Ocharan-Hernandez, Maria
Castillo-Henkel, Esther/ Castillo-Henkel, Enrique F.;
CORPORATE SOURCE: Carlos Seccion de Estudios de Posgrado e Investigacion, Escuela Superior de Medicina del Instituto Politecnico Nacional, Mexico, Mex.
SOURCE: Proceedings of the Western Pharmacology Society (1999), 42, 23-24
CODEN: WPFSA8; ISSN: 0083-8969
PUBLISHER: Western Pharmacology Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was noted that vascular reactivity may differ between regions of the same vessel. The aim of the study was to evaluate the possibility of segmental differences in rat aorta contraction induced by phenylephrine. Concn.-response curves to phenylephrine obtained in thoracic and abdominal aortic rings with or without endothelium did not differ quant.
IT 21102-95-4, RMY 7378
RL: BSU (Biological study, unclassified); BIOL (Biological study) (segmental differences in rat aorta contraction induced by phenylephrine)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



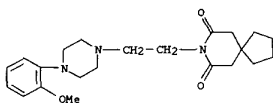
●2 HCl

REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 55 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 56 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:723048 CAPLUS
DOCUMENT NUMBER: 131:346557
TITLE: Method using .alpha.1D-adrenergic antagonists for treating bladder and lower urinary tract syndromes,
and screening method
INVENTOR(S): Schwinn, Debra A.
PATENT ASSIGNEE(S): Duke University, USA
SOURCE: PCT Int. Appl., 38 pp.
CODEN: PIXKD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:
PATENT NO. KIND DATE APPLICATION NO. DATE
WO 9957131 A1 19991111 WO 1999-US9846 19990506
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
CA 2327543 AA 19991111 CA 1999-2327543 19990506
AU 9938830 A1 19991123 AU 1999-38830 19990506
EP 1075486 A1 20010214 EP 1999-921690 19990506
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
JP 2002513799 T2 20020514 JP 2000-547100 19990506
PRIORITY APPLN. INFO.: US 1998-844792 P 19980506
WO 1999-US9846 W 19990506
AB The invention relates to bladder and lower urinary tract syndromes, particularly, irritative symptoms, and to a method of treating them using an .alpha.1D-adrenergic receptor (.alpha.1DAR) antagonists. Also provided is a method of screening compds. for their ability to serve as .alpha.1DAR selective antagonists.
IT 21102-95-4, RMY7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES

L14 ANSWER 56 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(Uses)
[.alpha.1b-adrenergic antagonists for treating bladder and lower
urinary tract syndromes, and screening method]
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

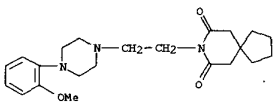


● 2 HCl

REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

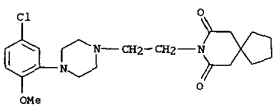
L14 ANSWER 57 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:709584 CAPLUS
DOCUMENT NUMBER: 131:310650
TITLE: Inverse agonism and neutral antagonism at
.alpha.1a-
and .alpha.1b-adrenergic receptor subtypes
AUTHOR(S): Rossier, Olivier; Abuin, Liliane; Fanelli,
Francesca;
CORPORATE SOURCE: Leonardi, Amedeo; Cotecchia, Susanna
Institute of Pharmacology and Toxicology,
Universite
de Lausanne, Lausanne, Switz.
SOURCE: Molecular Pharmacology (1999), 56(5), 858-866
CODEN: MOPMA3; ISSN: 0026-895X
PUBLISHER: American Society for Pharmacology and Experimental
Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have characterized the pharmacol. antagonism, i.e., neutral
antagonism
or inverse agonism, displayed by a no. of .alpha.-blockers at two
.alpha.1-adrenergic receptor (AR) subtypes, .alpha.1a- and
.alpha.1b-AR.
Constitutively activating mutations were introduced into the
.alpha.1a-AR
at the position homologous to A293 of the .alpha.1b-AR where
activating
mutations were previously described. Twenty-four .alpha.-blockers
differing in their chem. structures were initially tested for their
effect
on the agonist-independent inositol phosphate response mediated by the
constitutively active A271E and A293E mutants expressed in COS-7
cells. A
selected no. of drugs also were tested for their effect on the small,
but
measurable spontaneous activity of the wild-type .alpha.1a- and
.alpha.1b-AR expressed in COS-7 cells. The results of our study
demonstrate that a large no. of structurally different
.alpha.-blockers
display profound neg. efficacy at both the .alpha.1a- and .alpha.1b-AR
subtypes. For other drugs, the neg. efficacy varied at the different
constitutively active mutants. The most striking difference concerns
a
group of N-arylpiperazines, including
8-[2-[4-(5-chloro-2-methoxyphenyl)-1-
piperazinyl]ethyl]-8-azaspiro[4.5] decane-7,9-dione (REC 15/3039), REC
15/2739, and REC 15/3011, which are inverse agonists with profound
neg.
efficacy at the wild-type .alpha.1b-AR, but not at the .alpha.1a-AR.
IT 21102-95-4, RMY 7378 25240-56-5, REC 15/3039
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); BIOL (Biological study)
(inverse agonism and neutral antagonism at .alpha.1a- and
.alpha.1b-adrenergic receptor subtypes)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 57 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

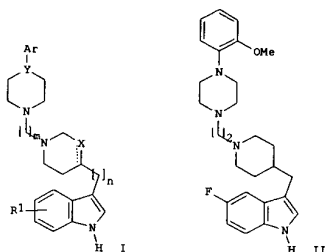
RN 252240-56-5 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione,
8-[2-[4-(5-chloro-2-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 58 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:708760 CAPLUS
DOCUMENT NUMBER: 131:310650
TITLE: Preparation of indolyl derivatives as serotonergic
agents
INVENTOR(S): Kelly, Michael Gerard; Kang, Young Hee
PATENT ASSIGNEE(S): American Home Products Corp., USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXKD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9956695 | A1 | 19991104 | WO 1999-US9181 | 19990428 |
| V: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2330437 | AA | 19991104 | CA 1999-2330437 | 19990428 |
| AU 9939670 | A1 | 19991116 | AU 1999-39670 | 19990428 |
| EP 1073651 | A1 | 20010207 | EP 1999-922739 | 19990428 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002513016 T2 20020508 JP 2000-545855 19990428 | | | | |
| PRIORITY APPL. INFO.: US 1998-69043 A 19980429 | | | | |
| WO 1999-US9181 W 19990428 | | | | |
| OTHER SOURCE(S): MARPAT 131:310650 | | | | |
| GI | | | | |



AB The title compds. [I; R1 = H, OH, OR2, halo (F, Cl, Br, I); R2 = lower alkyl; n = 0-2; X = CH, CH2; m = 2-4; Y = N, CH; Ar = (un)substituted aryl, heteroaryl] or their pharmaceutically acceptable salts, useful for the inhibition of serotonin uptake and the treatment of CNS disorders, particularly depression and anxiety. Thus, reaction of 4-(5-fluoro-1H-indol-3-ylmethyl)piperidine with 1-(2-chloroethyl)-4-(2-methoxyphenyl)piperazine in the presence of K2CO3 and XI in MeCN afforded 204 II which showed Ki of 4.8 nM against [3H]-paroxetine binding.

IT 247911-01-9P 247911-02-OP 247911-05-3P
247911-06-4P 247911-07-5P 247911-08-6P
247911-09-7P 247911-12-2P 247911-14-4P
247911-15-5P 247911-16-6P

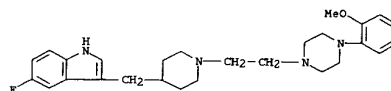
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of indolyl derivs. as serotonergic agents)

RN 247911-01-9 CAPLUS

CN 1H-Indole,

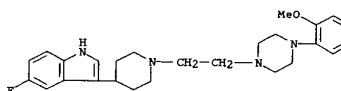
5-fluoro-3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]methyl]- (9CI) (CA INDEX NAME)



RN 247911-02-0 CAPLUS

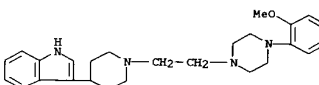
CN 1H-Indole,

5-fluoro-3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



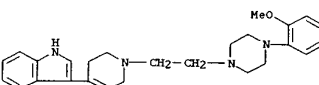
RN 247911-05-3 CAPLUS

CN 1H-Indole, 3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



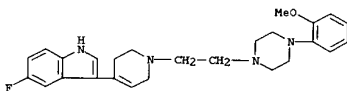
RN 247911-06-4 CAPLUS

CN 1H-Indole, 3-[[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]- (9CI) (CA INDEX NAME)



RN 247911-07-5 CAPLUS

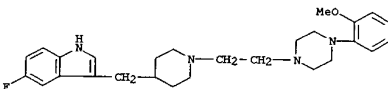
CN 1H-Indole, 5-fluoro-3-[[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]- (9CI) (CA INDEX NAME)



RN 247911-08-6 CAPLUS

CN 1H-Indole,

5-fluoro-3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]methyl]-, dihydrochloride (9CI) (CA INDEX NAME)

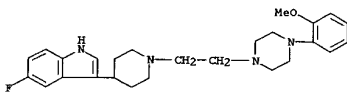


● 2 HCl

RN 247911-09-7 CAPLUS

CN 1H-Indole,

5-fluoro-3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

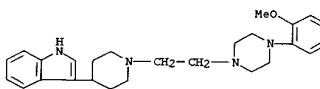
RN 247911-12-2 CAPLUS

CN 1H-Indole, 3-[[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

CRN 247911-05-3

CMF C26 H34 N4 O



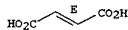
CH 2

CRN 110-17-8

CMF C4 H4 O4

CDES 2:E

Double bond geometry as shown.



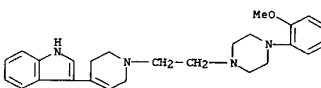
RN 247911-14-4 CAPLUS

CN 1H-Indole, 3-[[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]-, (2E)-2-butenedioate (2:1) (9CI) (CA INDEX NAME)

CH 1

CRN 247911-06-4

CMF C26 H32 N4 O



CH 2

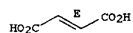
CRN 110-17-8

CMF C4 H4 O4

CDES 2:E

Double bond geometry as shown.

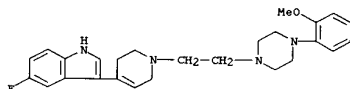
L14 ANSWER 58 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 247911-15-5 CAPLUS
CN 1H-Indole,
5-fluoro-3-[1,2,3,6-tetrahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-pyridinyl]-, (2E)-2-butenedioate (1:2) (9CI)
(CA INDEX NAME)

CM 1

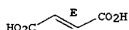
CRN 247911-07-5
CMF C26 H31 F N4 O
CDES 2:E



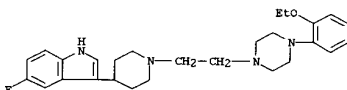
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 247911-16-6 CAPLUS
CN 1H-Indole,
3-[1-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-5-fluoro- (9CI) (CA INDEX NAME)

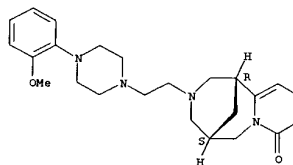


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS

L14 ANSWER 59 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:571555 CAPLUS
DOCUMENT NUMBER: 131:337220
TITLE: Synthesis and preliminary pharmacological evaluation of some cytosine derivatives
AUTHOR(S): Boido, Caterina Canu Sparatore, Fabio
CORPORATE SOURCE: Dipartimento di Scienze Farmaceutiche, Universita di Genova, Genoa, 3-16132, Italy
SOURCE: Farmaco (1999), 54(7), 438-451
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Thirty-one N-derivs. of cytosine were prepd. to modify the pharmacol. profile and to obtain compds. of potential therapeutic interest either at a peripheral or central level, particularly as nicotinic ligands with improved ability to cross the blood-brain barrier. With the introduction of different kinds of substituents on the basic nitrogen of cytosine a variety of activities were obsd., both in vivo (analgesic, dopamine antagonism, antihypertensive, inhibition of stress-induced ulcers, antiinflammatory, protection from PAF-induced mortality, hypoglycemic) and in vitro (pos. cardio-inotropic, .beta.-adrenergic antagonism, .alpha.1- and .alpha.2-antagonism, inhibition of PAF-induced platelet aggregation). Six randomly selected compds. were tested for the ability to recognize a central nicotinic receptor and four of them exhibited KI values in the range 30-163 nM.
IT 249907-28-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. of cytosine derivs. and their preliminary pharmacol. evaluation)
RN 249907-28-6 CAPLUS
CN 1,5-Methano-8H-pyrido[1,2-a][1,5]diazocin-8-one, 1,2,3,4,5,6-hexahydro-3-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

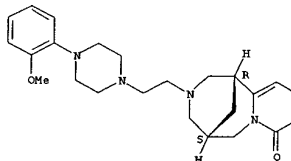
L14 ANSWER 59 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT



●2 HCl

IT 249906-94-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of cytosine derivs. and their preliminary pharmacol. evaluation)
RN 249906-94-3 CAPLUS
CN 1,5-Methano-8H-pyrido[1,2-a][1,5]diazocin-8-one, 1,2,3,4,5,6-hexahydro-3-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (1R,5S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

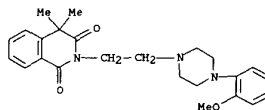
L14 ANSWER 60 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:565907 CAPLUS
DOCUMENT NUMBER: 131:194295
TITLE: Agents, and combinations thereof, with serotonin-related activity for the treatment of sleep-related breathing disorders
INVENTOR(S): Radulovacki, Miodrag; Carley, David W.
PATENT ASSIGNEE(S): The Board of Trustees of the University of Illinois,
SOURCE: USA
PCT Int. Appl., 46 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9943319 | A1 | 19990902 | WO 1999-US4347 | 19990226 |
| W: CA, JP, US | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, | | | | |
| NL, PT, SE | | | | |
| CA 2321900 | AA | 19990902 | CA 1999-2321900 | 19990226 |
| EP 1066036 | A1 | 20010110 | EP 1999-909664 | 19990226 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, | | | | |
| PT, IE, FI | | | | |
| JP 2002504510 | T2 | 20020212 | JP 2000-533116 | 19990226 |
| US 6331536 | B1 | 20011218 | US 2000-622823 | 20000823 |
| US 2002086870 | A1 | 20020704 | US 2001-16901 | 20011214 |
| PRIORITY APPLN. INFO.: US 1998-76216P P 19980227 | | | | |
| WO 1999-US4347 W 19990226 | | | | |
| US 2000-622823 A1 20000823 | | | | |

AB Pharmacol. methods are provided for the prevention or amelioration of sleep-related breathing disorders via administration of agents or combinations of agents that possess serotonin-related pharmacol. activity.
IT 67339-62-2, ARC239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(agents, and combinations thereof, with serotonin-related activity for treatment of sleep-related breathing disorders)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-isouquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

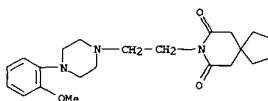
L14 ANSWER 61 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:547948 CAPLUS
DOCUMENT NUMBER: 131:281021
TITLE: Effect of several 5-hydroxytryptamine_{1A} receptor ligands on the micturition reflex in rats:
comparison with WAY 100635
AUTHOR(S): Testa, R.; Guarneri, L.; Poggesi, E.; Angelico, F.;
Riva, C.; Velasco, C.; Ibbas, M.; Cilia, A.; Motta, G.;
CORPORATE SOURCE: Leonardi, A.
Pharmaceutical Research and Development Division,
Milan, Italy
SOURCE: Journal of Pharmacology and Experimental
Therapeutics
(1999), 290(3), 1258-1269
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and
Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several novel N-arylpiperazine derivs. were synthesized and tested for their (1) affinity and functional activity on 5-hydroxytryptamine_{1A} (5-HT_{1A}) receptors in vitro; (2) activity in models predictive of antagonism at somatodendritic and postsynaptic 5-HT_{1A} receptors; (3) and effects on the micturition reflex in anesthetized and conscious rats. These studies also included 1-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl]piperazine hydrobromide (NAN 190), 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4,5]decane-7, 9-dione dihydrochloride (RMV 7378), and N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-N-[2-pyridinyl]cyclohexanecarboxamide (WAY 100635). Almost all compds. were found to be potent and selective for the human recombinant 5-HT_{1A} receptor, with K_i values in the nanomolar range. [35S]GTP.gamma.S binding in HeLa cells expressing the recombinant human 5-HT_{1A} receptor allowed classification of the compds. into neutral antagonists and partial agonists. Almost all neutral antagonists were active in blocking 8-hydroxy-2-dipropylamnotetralin (8-OH-DPAT)-induced forepaw treading in rats (postsynaptic model) and hypothermia in mice (somatodendritic model) with the same potency, whereas compds. showing partial agonistic activity were active in the postsynaptic model but were inactive, or poorly active, in the somatodendritic model. Neutral antagonists potently inhibited vol.-induced bladder-voiding contractions in anesthetized rats. Contractions were completely blocked, and the disappearance of bladder

L14 ANSWER 60 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 61 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
contractions lasted 7 to 13 min after the highest doses tested. Furthermore, neutral antagonists increased bladder vol. capacity in conscious rats during continuous transvesical cystometry, whereas micturition pressure was only slightly, and not dose-dependently, reduced. Partial agonists were inactive or poorly active, inducing a disappearance time of bladder contractions that did not exceed 6 min in anesthetized rats, and failing to increase bladder vol. capacity in conscious rats. These findings indicate that only neutral 5-HT_{1A} receptor antagonists are endowed with inhibitory effects on the bladder.
IT 21102-95-4, RMY 7378
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(N-arylpiperazine derivs. affinity at 5-HT_{1A} receptor and other G protein-coupled receptors and effects 5-HT_{1A} receptor ligands on micturition reflex in rats)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



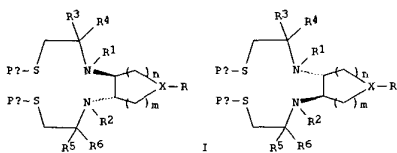
● 2 HCl

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

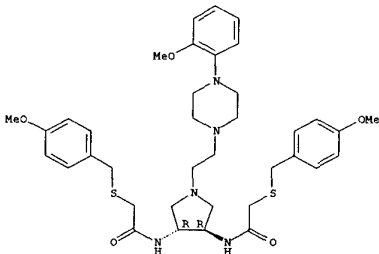
L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:528991 CAPLUS
DOCUMENT NUMBER: 131:153032
TITLE: Preparation of diaminedithiol stereoselective
ligands
use to complex with technetium-99m pertechnetate for
as radioimaging agents
INVENTOR(S): Kung, Hank F.; Kung, Mei-ping; Zhuang, Zhi-ping
PATENT ASSIGNEE(S): Trustees of the University of Pennsylvania, USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| WO 9940882 | A2 | 19990819 | WO 1999-US2513 | 19990205 |
| WO 9940882 | A3 | 19991104 | | |

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.: US 1998-73957P P 19980206
US 1998-78052P P 19980316
OTHER SOURCE(S): MARPAT 131:153032
GI

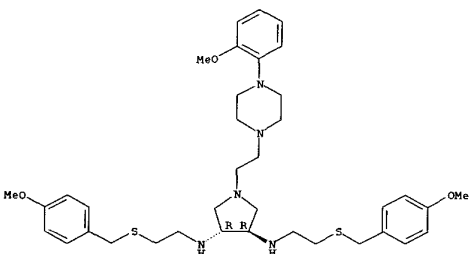


L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 235098-40-5 CAPLUS
CN 3,4-Pyrrolidinediamine,
N,N'-bis[2-[[[(4-methoxyphenyl)methyl]thio]ethyl]-1-
[2-[[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (3R,4R)- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.



IT 235098-41-6P
RL: SPN (Synthetic preparation); PREP (Preparation)

L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

AB The present invention concerns novel diaminedithiol pyrrolidine deriv.
ligands, represented by Formulas I and II, that form complexes with a
radioactive metal through a chelate bond. The complexes are useful in
radiodiagnostic compns. employed for imaging. In said ligand

formulas, X
= N or CH, R1 and R2 are selected from H or (un)substituted alkyl or
aralkyl where at least one of R1 and R2 is H, R3 and R4 are H or
together
form a keto group, R5 and R6 are H or together form a keto group, m
and n
are independently 1 or 2, R = H, (un)substituted C1-6 alkyl, C3-7
cycloalkyl, or C6-10ar(C1-4)alkyl, and Pa = sulfur protecting group
or H.

In addn., R in the formulas above may be -L-B where L is a linking
group,
e.g., alkyl, amido, hydrazino, etc., and B is a targeting group, e.g.,
amino acid, peptide, protein, antibody, nucleic acid, steroid, lipid,
saccharide, or cell membrane ligand. Radionuclide complexes of I and

II
are claimed, e.g., with Tc-99m, Re-186, and Re-188. The compds. of
the
invention avoid the formation of diastereomer mixts. based on
incorporating [TcVO]+3N2S2 as a chelating moiety since these compds.
form

only one isomer when complexed with [99mTcVO4]+. A process for
radioimaging with the radionuclide complexes and a kit for forming an
injectable radiopharmaceutical compn. contg. I and II are claimed.
Examples are provided for the prepn. of the stereoselective ligands,
e.g.,

(3R,4R)-I (X = N, R = PhCH2, Pa = R1 = R2 = R3 = R4 = H, n = m = 1),
its
radiolabeling with [99mTc]pertechnetate, and its biodistribution in
rats,
which showed good heart uptake.

IT 235098-39-2P 235098-40-5P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

RACT (Reactant or reagent)

(for prepn. of chiral diaminedithiol pyrrolidine deriv. as chelate
ligand with radionuclides used as radioimaging agents)

RN 235098-39-2 CAPLUS

CN Acetamide,

N,N'-[(3R,4R)-1-(2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-
3,4-pyrrolidinediyl]bis[2-[[[(4-methoxyphenyl)methyl]thio]- (9CI) (CA
INDEX NAME)

Absolute stereochemistry.

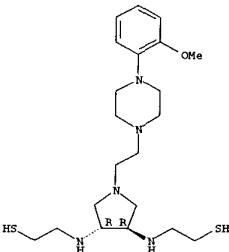
L14 ANSWER 62 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(prepn. as chelate ligand with radionuclides used as radioimaging
agents)

RN 235098-41-6 CAPLUS

CN Ethanethiol,

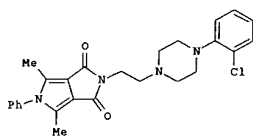
2,2'-[[[(3R,4R)-1-(2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl)-
3,4-pyrrolidinediyl]diimino]bis- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



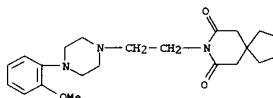
L14 ANSWER 63 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:494795 CAPLUS
 DOCUMENT NUMBER: 131:295533
 TITLE: Importance of agonists in .alpha.-adrenoceptor classification and localization of .alpha.1-adrenoceptors in human prostate
 AUTHOR(S): McGrath, J. C.; Naghadeh, M. A.; Pediani, J. D.; Mackenzie, J. F.; Daly, C. J.
 CORPORATE SOURCE: Autonomic Physiology Unit, Division of Neurosciences and Biomedical Systems, and Institute of Biomedical and Life Sciences, University of Glasgow, Glasgow, G12 8QQ, UK
 SOURCE: European Urology (1999), 36(Suppl. 1), 80-88
 CODEN: EUURAV; ISSN: 0302-2838
 PUBLISHER: S. Karger AG
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB .alpha.-Adrenoceptor blocker drugs are commonly used in the clin. (non-surgical) treatment of BPH. .alpha.1-Adrenoceptors were originally sub-divided using agonists but, subsequently, were sub-divided using only antagonists in ligand-ligand interactions, which did not require agonists at all. Ultimately, proof that adrenoceptors are functional receptors for the natural ligands, noradrenaline and adrenaline, requires that agonists be used. The earlier excitement engendered by finding varying agonist potency series in different tissues has not been revisited to place it in the context of current concepts of .alpha.1-adrenoceptor subtypes. This review will consider the advantages and limitations of different agonists for the study of .alpha.1-adrenoceptor subtypes including "extreme" examples where the archetypal .alpha.1-adrenoceptor agonist phenylephrine activates .alpha.2-adrenoceptors and others where UK14304, often the .alpha.2-adrenoceptor agonist of choice, activates .alpha.1-adrenoceptors. New work will also be presented showing the interaction between agonists and the fluorescent .alpha.1-adrenoceptor antagonist QAPB. This introduces the novel point of view of studying the displacement of antagonists by agonists. Possible errors in antagonist classification arising from complexity in the actions of agonists and the recently developed method of fluorescent ligand binding on isolated living human prostatic smooth muscle cells will be discussed.
 IT 21102-95-4, EMY7378
 RL: PAC (Biological activity or effector, except adverse); BPR (Biological

L14 ANSWER 64 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:470679 CAPLUS
 DOCUMENT NUMBER: 131:228607
 TITLE: Synthesis and pharmacological screening of some N-(4-substituted-piperazin-1-ylalkyl)-3,4-pyrroledicarboximides
 AUTHOR(S): Rajtar, Malinka, Wieslaw; Sieklucka-Dziuba, Maria;
 CORPORATE SOURCE: Grazyna; Rubaj, Andrzej; Kleinrok, Zdzislaw
 University Department of Chemistry of Drugs, Wroclaw
 SOURCE: of Medicine, Wroclaw, 50-137, Pol. Farmaco (1999), 54(6), 390-401
 CODEN: FRMCES; ISSN: 0014-827X
 PUBLISHER: Elsevier Science S.A.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 131:228607
 GI



AB The synthesis and pharmacol. investigation of a new series of derivs. of pyrrole-3,4-dicarboximide, e.g. I, possessing the 4-substituted-piperazin-1-ylalkyl group linked to the imide nitrogen is presented. The products were evaluated for acute toxicity, and effectiveness in a series of CNS and arterial blood pressure tests. The preliminary pharmacol. screening was detd. in animal models. Several compds. demonstrated moderate to high analgesic activity in the "writhing syndrome" test (Sf-1/640 LD50). Some of the structure-activity relationships are also discussed.
 IT 244006-90-4P 244006-92-6P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. of piperazinylalkylpyrroledicarboximides with evaluation of depressant and analgesic activity)

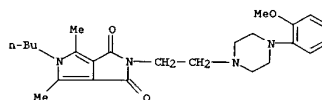
L14 ANSWER 63 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (importance of agonists in .alpha.-adrenoceptor classification and localization of .alpha.1-adrenoceptors in human prostate)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



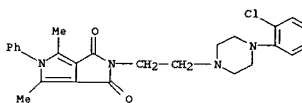
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REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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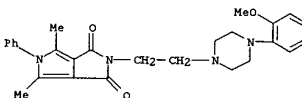
L14 ANSWER 64 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 244006-90-4 CAPLUS
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 2-butyl-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)



RN 244006-92-6 CAPLUS
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl-5-phenyl- (9CI) (CA INDEX NAME)

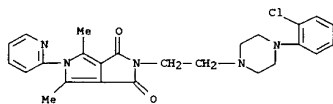


IT 244006-91-5P 244006-93-7P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of piperazinylalkylpyrroledicarboximides with evaluation of depressant and analgesic activity)
 RN 244006-91-5 CAPLUS
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,6-dimethyl-5-phenyl- (9CI) (CA INDEX NAME)



RN 244006-93-7 CAPLUS
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl-5-(2-pyridinyl)- (9CI) (CA INDEX NAME)

L14 ANSWER 64 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

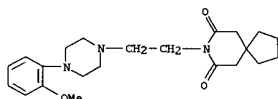


REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 65 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:449795 CAPLUS
DOCUMENT NUMBER: 131:223799
TITLE: Analysis of .alpha.1-adrenoceptor subtypes in rabbit
aorta and arteries: regional difference and co-existence
AUTHOR(S): Satoh, Mitsutoshi; Enomoto, Keisuke; Takayanagi, Issei; Koike, Katsuo
CORPORATE SOURCE: Department of Chemical Pharmacology, Toho University
Japan
SOURCE: School of Pharmaceutical Sciences, Funabashi, Japan
European Journal of Pharmacology (1999), 374(2), 229-240
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This study was done to det. the .alpha.1-adrenoceptor subtypes and to characterize the functional role of .alpha.1D-adrenoceptors in the following rabbit arteries: thoracic and abdominal aorta, mesenteric, renal and iliac arteries. In all arteries, selective .alpha.1D-adrenoceptor antagonist BMY 7378 dose dependently shifted the concn.-response curves for norepinephrine to the right. Schild plots of the results obtained from the inhibition by BMY 7378 for norepinephrine yielded a straight line with a slope of unity in thoracic (pA2 6.54) and abdominal (pA2 6.73) aorta. Slopes of Schild plots obtained from the inhibition by BMY 7378 for norepinephrine were significantly different from unity in mesenteric, renal and iliac arteries. Slopes of Schild plots for BMY 7378 were not different from unity in chloroethylclonidine-treated thoracic (pA2 6.49) and abdominal (pA2 6.61) aorta. Slopes of Schild plots for BMY 7378 were significantly different from unity in chloroethylclonidine-treated mesenteric, renal and iliac arteries. On the other hand, in Ca2+-free physiol. saline soln. (Ca2+-free PSS) slopes obtained from Schild plots for BMY 7378 were not different from unity in thoracic (pA2 6.41) and abdominal (pA2 6.28) aorta and mesenteric (pA2 6.55), renal (pA2 6.24) and iliac (pA2 6.64) arteries. BMY 7378 inhibited [3H]prazosin binding to thoracic (pKi 6.44) and abdominal (pKi 6.59) aorta with low potency, and mesenteric (pKi High 8.66, pKi Low 6.34), renal (pKi High 8.71, pKi Low 6.45) and iliac artery (pKi High 8.60, pKi Low 6.56). These results suggest that .alpha.1D-adrenoceptors play a significant role for contractile responses in renal and iliac artery, but play virtually no role in thoracic and abdominal aorta and that an .alpha.1-adrenoceptor subtype, which is pharmacol. distinguishable from the .alpha.1A-,

L14 ANSWER 65 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
.alpha.1B- and .alpha.1D-adrenoceptor subtype, may co-exist in mesenteric artery.
IT 21102-95-4, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(.alpha.1-adrenoceptor subtype pharmacol. characterization in rabbit aorta and arteries and regional differences and co-existence therein)
RN 21102-95-4 CAPLUS
CN 8-Azaspino[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



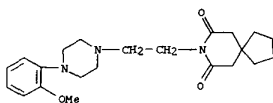
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REFERENCE COUNT: 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L14 ANSWER 66 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1999:437513 CAPLUS
DOCUMENT NUMBER: 131:194652
TITLE: Microphysiometric analysis of human .alpha.1A-adrenoceptor expressed in Chinese hamster ovary cells
AUTHOR(S): Taniguchi, Takanobu; Inagaki, Rika; Murata, Satoshi
Akiba, Isamu; Muramatsu, Ikunobu
CORPORATE SOURCE: Department of Pharmacology, Fukui Medical University,
Fukui, 910-1193, Japan
SOURCE: British Journal of Pharmacology (1999), 127(4), 962-968
CODEN: BJPCRM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The human recombinant .alpha.1A-adrenoceptor (AR) has been stably expressed in Chinese hamster ovary cells. Four stable clones, aH4, aH5, aH6 and aH7, expressing 30, 370, 940 and 2900 fmol AR mg-1 protein, resp., have been employed to characterize this AR subtype using radioligand binding and microphysiometry to measure extracellular acidification rates. Noradrenaline (NA) gave concn.-dependent responses in microphysiometry with increasing extracellular acidification rates. The potency of NA increased as the receptor d. increased; pEC50 values of NA for the clones aH4, aH5, aH6 and aH7 were 6.9, 7.5, 7.8 and 8.1, resp. This increase of potency according to receptor d. indicates the presence of spare receptor for NA. Methoxamine, phenylephrine, oxymetazoline and clonidine also gave concn.-dependent responses with various intrinsic activities. Antagonists shifted concn.-response curves for NA rightward in a concn.-dependent manner. Schild anal. revealed that the affinity profile of this AR subtype to antagonists in the clone aH7 had a typical pattern for the .alpha.1A-AR: high affinity for prazosin and WB 4101, and low affinity for BMY 7378 (pA2=9.5, 9.8 and 7.3, resp.). This profile is similar in the case of the clone aH4. These affinities were in good agreement with those obtained in binding expts. These results have demonstrated that (1) classical receptor theory can be applied in microphysiometry, and (2) microphysiometry is a useful tool to investigate the pharmacol. characterization of .alpha.1A-AR.
IT 21102-95-4, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(microphysiometry in pharmacol. characterization of human

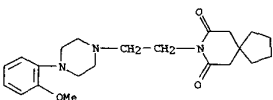
L14 ANSWER 66 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 .alpha.1a-adrenoceptor expressed in Chinese hamster ovary cells)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 67 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 and expression in vascular smooth muscle cell line cloned from p53
 knockout mice)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



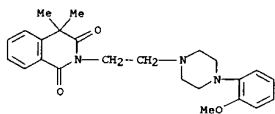
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REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 67 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:385955 CAPLUS
DOCUMENT NUMBER: 131:139836
TITLE: Characterization of .alpha.1-adrenoceptors expressed in a novel vascular smooth muscle cell line cloned from p53 knockout mice, P53LMAC01 (AC01) cells
AUTHOR(S): Ohmi, Kazuhiro; Shinoura, Hitomi; Nakayama, Yasuhisa;
CORPORATE SOURCE: Goda, Nobuhito; Tsujimoto, Gozoh
Medical Department of Pathology, National Children's
SOURCE: Research Center, Tokyo, 154-8509, Japan
British Journal of Pharmacology (1999), 127(3), 756-762
CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We pharmacol. studied the .alpha.1-adrenoceptor (AR) subtype(s) involved in receptor-mediated signaling in a novel vascular smooth muscle cell line cloned from p53 knockout mice, P53LMAC01 (AC01) cells. Radioligand binding studies with [125I]-HEAT showed the existence of a homogeneous population of binding site with an affinity (Kd value) of 0.4 nM and a max. no. of binding sites (Bmax) of 100 fmol mg-1 protein. Catecholamines competed for [125I]-HEAT binding stereospecifically and with the characteristic .alpha.1-AR potency series. Displacement curves for BMY-7378 and KMD-3213 best fitted a one-site model with a pKi value (-log10 (equil. inhibition const.)) of 6.06 and 7.07, resp. Reverse transcription-polymerase chain reaction (RT-PCR) assay detected .alpha.1B- and .alpha.1D-AR, but not .alpha.1A-AR transcript. Chlorethylclonidine (CEC) treatment nearly abolished (-)noradrenaline (NA) (10 .mu.M)-induced inositol[1,4,5]trisphosphate (IP3) prodn., and BMY-7378 inhibited the response with a Ki value of 0.3 nM, which value was similar to that obtained in the cells expressing .alpha.1D-AR. In both AC01 cells and cells expressing .alpha.1D-AR, BMY-7378 protected .alpha.1-ARs from CEC alkylation while it had little protective effect on CEC alkylation and NA-induced IP3 prodn. in cells expressing .alpha.1B-AR. The results indicate that AC01 cells contain predominantly .alpha.1B-ARs and a small population of .alpha.1D-ARs; however, phosphoinositide (PI)/Ca2+ signaling is mainly mediated through the minor population of .alpha.1D-ARs, rather than the .alpha.1B-ARs.
IT 21102-95-4, BMY-7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.1-adrenoceptor subtype functional pharmacol. characterization

L14 ANSWER 68 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:363284 CAPLUS
DOCUMENT NUMBER: 131:111771
TITLE: Functional .alpha.2C-adrenoceptors in human neuroblastoma SH-SY5Y cells
AUTHOR(S): Parsley, Stephanie; Gazi, Lucien; Bobirac, Ionel; Loetscher, Erika; Schoeffter, Philippe
CORPORATE SOURCE: Nervous System Therapeutic Area, Novartis Pharma Research, Basel, CH-4002, Switz.
SOURCE: European Journal of Pharmacology (1999), 372(1), 109-115
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The .alpha.2-adrenoceptor mediating inhibition of forskolin-stimulated cAMP accumulation in human neuroblastoma SH-SY5Y cells was further characterized. The .alpha.2-adrenoceptor agonists, UK 14,304 (5-bromo-6-(2-imidazolin-2-ylamino)quinoline), oxmetazoline, guanfacine, (-)noradrenaline and clonidine concn.-dependently decreased cAMP accumulation in this cell line (Emax .apprx.50% inhibition). Agonist pEC50 values ranged between 6.7 and 7.8. Clonidine was a partial agonist. The effects of UK 14,304 were blocked after a pertussis toxin treatment. The concn.-response curves of UK 14,304 were shifted to the right in a parallel manner by the following antagonists (mean pKB values): yohimbine (8.17), idazoxan (7.63), prazosin (6.66), 2-[2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl]-4,4-dimethyl-1,3-(2H,4H) isoquinolinedione (ARC 239; 7.12) and 2-(2,6-dimethoxyphenoxylethyl)aminomet hyl-1,4-benzodioxane (WB-4101; 8.12). The relatively high pKB values of prazosin and ARC 239 point to a non-.alpha.2A-adrenoceptor-mediated effect. The relatively high pKB value of WB-4101 further characterizes the .alpha.2-adrenoceptor in SH-SY5Y cells as being of the .alpha.2C subtype. The anal. of the expression of .alpha.2-adrenoceptor subtypes by reverse transcriptase-polymerase chain reaction (RT-PCR) revealed the exclusive presence of .alpha.2C-adrenoceptor mRNA in SH-SY5Y cells. The authors propose that inhibition of forskolin-stimulated cAMP accumulation in SH-SY5Y cells be used as a functional model of human, native .alpha.2C-adrenoceptors.
IT 67339-62-2, ARC 239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (.alpha.2-adrenoceptors characterization in human neuroblastoma SH-SY5Y cell by .alpha.2-adrenoceptor agonist and antagonist)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 68 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE
FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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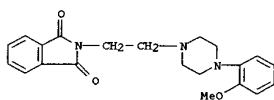
L14 ANSWER 69 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:282212 CAPLUS
DOCUMENT NUMBER: 130:311818
TITLE: Preparation of arylpiperazines as serotonin
reuptake inhibitors and 5-HT1D.alpha. antagonists
INVENTOR(S): Walker, Clint Duane; Wong, David Taiwai; Xu,
Yao-Chang
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 61 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|---|----------|-------------------|----------|
| WO 9920621 | A1 | 19990429 | WO 1998-US22265 | 19981021 |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, T.J, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2307114 | AA | 19990429 | CA 1998-2307114 | 19981021 |
| AU 9911931 | A1 | 19990510 | AU 1999-11931 | 19981021 |
| EP 1028958 | A1 | 20000823 | EP 1998-955031 | 19981021 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | |
| JP 2001520225 | T2 | 20011030 | JP 2000-516963 | 19981021 |
| US 6342498 | B1 | 20020129 | US 2000-509957 | 20000331 |
| PRIORITY APPLN. INFO.: | | | US 1997-63493F | 19971022 |
| | | | WO 1998-US22265 | 19981021 |
| OTHER SOURCE(S): | | | MARPAT 130:311818 | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1, R2 = H, halo, alkyl, etc.; R3 = H, alkyl; Y = CO, CH2; Z = NH, C(COR), CH2; R = alkyl, cycloalkyl; n, m = 1-3] and their salts, serotonin reuptake inhibitors and 5-HT1D.alpha. receptor

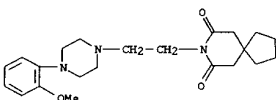
L14 ANSWER 69 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
antagonists useful in the treatment of depression and anxiety, were
prep.d. and formulated. E.g., a 4-step synthesis of piperazine II, starting
with 1-(2-methoxyphenyl)piperazine, was given. Representative compds. I
showed Ki at the 5-HT1A and 5-HT1D.alpha. receptors of at least 300 .mu.M.
IT 997118-67-99
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(prepn. of arylpiperazines as serotonin reuptake inhibitors and
5-HT1D.alpha. antagonists)
RN 997118-67-9 CAPLUS
CN 1H-isoindole-1,3(2H)-dione,
2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR
THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L14 ANSWER 70 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1999:203816 CAPLUS
DOCUMENT NUMBER: 131:27831
TITLE: New .alpha.1-adrenoceptor antagonist, JTH-601,
shows more than 10 times higher affinity for human
prostates than arteries
AUTHOR(S): Takahashi, Masahiko; Taniguchi, Takanobu; Murata,
Satoshi; Okada, Kenichiro; Moriyama, Nobuo;
Yamazaki, Satoru; Muramatsu, Ikunobu
CORPORATE SOURCE: Departments of Pharmacology and Urology, School of
Medicine, Fukui Medical University, Fukui,
910-1193,
Japan
SOURCE: Journal of Urology (Baltimore) (1999), 161(4),
1350-1354
CODEN: JOURAA; ISSN: 0022-5347
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The authors compared the affinities of a new .alpha.1-adrenoceptor
(AR) antagonist, JTH-601 with those of several .alpha.1-AR antagonists in
human prostates and arteries. In the functional study, noradrenaline
produced concn.-dependent contractions in human prostates and mesenteric
arteries. The pA2/pKB values for the antagonists in the human prostate were
9.78 for tamsulosin, 8.84 for JTH-601, 8.39 for WB4101, 8.23 for prazosin,
8.12 for JTH-601-G1 (a main metabolite of JTH-601 in human) and 6.57 for
BMJ7378. Compared these affinities with those in the mesenteric artery, only
JTH-601 and JTH-601-G1 exhibited unique uroselectivity, showing 10- to
20-fold higher affinity for the human prostate than for mesenteric
artery. The affinity profile of these antagonists suggested that the
noradrenaline induced contractions in the human prostate and the mesenteric artery
were mediated by the .alpha.1L-AR and .alpha.1B-AR, resp. In the
competition binding study, the pharmacol. profiles of the antagonists against
[3H]-prazosin were examd. in the human prostate and aorta. The
resulting pKi values for JTH-601 and JTH-601-G1 were also approx. 10- to 20-fold
higher for the human prostate than for the human aorta. These results
have suggested that JTH-601 and JTH-601-G1 are unique uroselective
.alpha.1-AR antagonists that show higher affinity for the human
prostate than for the human arteries.
IT 21102-95-4, BMJ7378
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological

L14 ANSWER 70 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 study, unclassified); BIOL (Biological study)
 (.alpha.1-adrenoceptor antagonist JTH-601 affinity comparison with
 those of several .alpha.1-AR antagonists for human prostates and
 arteries)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

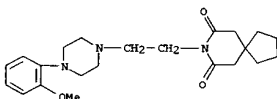


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REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 71 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:186984 CAPLUS
 DOCUMENT NUMBER: 131:30042
 TITLE: Differences of antagonism for a selective
 .alpha.1D-adrenoceptor antagonist BMY 7378 in the
 rabbit thoracic aorta and iliac artery
 Satoh, Mitsutoshi; Enomoto, Katsuko; Takayanagi,
 Issei; Koike, Katsuo
 CORPORATE SOURCE: Department of Chemical Pharmacology, Toho
 University
 School of Pharmaceutical Sciences, Chiba,
 274-8510,
 Japan
 SOURCE: Journal of Smooth Muscle Research (1998), 34(4),
 151-158
 CODEN: JSMRE2; ISSN: 0916-8737
 PUBLISHER: Japanese Society of Smooth Muscle Research
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Based on the affinity of .alpha.1D-adrenoceptor subtype for a
 selective
 antagonist BMY 7378, we studied its functional role in rabbit thoracic
 aorta and iliac artery, and evaluated the subtypes of the
 .alpha.1-adrenoceptors that are activated by phenylephrine (a full
 agonist) and tizanidine (a partial agonist). In thoracic aorta, the
 concn.-response curves of phenylephrine and tizanidine were
 antagonized by
 BMY 7378 with low potency (pA2 values 6.68+/-0.06 and 6.67+/-0.06,
 slopes of Schild plot 1.06+/-0.04 and 1.01+/-0.04, resp.). On the
 other
 hand, in iliac artery concn.-response curves for phenylephrine were
 potentially antagonized by a low concn. of BMY 7378, and the slope
 (0.75+/-0.02) of the Schild plot was significantly different from
 unity.
 In iliac artery, a concn.-response curve of tizanidine was
 antagonized by
 BMY 7378 with low potency (pA2 value 6.64+/-0.08, slope of Schild
 plot 1.01+/-0.05). These results suggest that an .alpha.1D-adrenoceptor
 subtype contributes to .alpha.1-adrenoceptor mediating muscle
 contraction
 in iliac artery, but not in thoracic aorta of rabbit, and that it is
 activated by a full agonist phenylephrine but not by a partial agonist
 tizanidine.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); BIOL (Biological study)
 (antagonism difference for selective .alpha.1D-adrenoceptor
 antagonist
 BMY 7378 in thoracic aorta and iliac artery)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 71 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

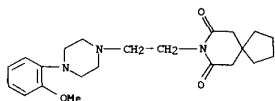


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REFERENCE COUNT: 15 THERE ARE 15 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 72 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:127244 CAPLUS
 DOCUMENT NUMBER: 131:13770
 TITLE: Modification of sexual behavior of Long-Evans male
 rats by drugs acting on the 5-HT1A receptor
 Rehman, Jamil; Kaynan, Ayali; Christ, George;
 Valcic,
 Mira; Maayani, Saul; Melman, Arnold
 CORPORATE SOURCE: Department of Urology, Albert Einstein College of
 Medicine/Montefiore Medical Center, Bronx, NY,
 10467,
 USA
 SOURCE: Brain Research (1999), 821(2), 414-425
 CODEN: BRREAP; ISSN: 0006-8993
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Modulation of the sexual behavior of male rats by the anxiolytic
 buspirone
 (S-20499) and its analog gepirone were compared to the effects of
 8-OH-DPAT (or DPAT, a selective 5-HT1A ref. agonist), and BMY-7378 (a
 selective 5-HT1A partial agonist). Long-Evans rats were used;
 modulation
 of copulatory behavior and alteration of penile reflexes were examd.
 Modulation of copulatory behavior was assessed by three indexes:
 frequency
 and length of intromission, and latency of ejaculation. DPAT, at
 doses of
 1-8 mg/kg, reduced these three indexes in a time dependent manner such
 that the effects peaked at 45 min and normalized at 90 min. The
 dose-effect relation (assessed 45 min after DPAT injection) is
 bell-shaped
 with an ED50 approx. 1 mg/kg on the ascending limb of the curve. The
 effects of buspirone (2 mg/kg) and gepirone (2 mg/kg) on copulatory
 behavior were indistinguishable from control. BMY-7378 alone and in
 combination with these other 5-HT1A agonists reduced copulatory
 behavior,
 though not statistically significant. Penile reflexes, including no.
 of
 erections, cups and flips, were inhibited by these agents:
 DPAT>buspirone>gepirone (inactive at 2 mg/kg). Furthermore, the
 latency
 period to erection was at least doubled by DPAT (2 mg/kg). Buspirone
 and
 gepirone, however, reduced the latency period to erection. BMY-7378
 inhibited penile reflexes when administered alone and even more in
 combination with DPAT or buspirone. Two butyrophenone analogs,
 spiperone
 (a 5-HT1A and dopamine D2 antagonist) and haloperidol (a D2
 antagonist),
 were also tested for their interaction with DPAT. Both of these
 drugs (at
 0.25 mg/kg, 60 min after administration) reduced all indexes of penile
 reflexes and copulation. Furthermore, in combination with DPAT (2
 mg/kg,
 45 min), the effects were synergistic such that sexual activity came
 nearly to a standstill. These opposing effects on putatively brain

L14 ANSWER 72 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 originated copulatory behavior and spinal mediated penile reflexes
 indicate that the effects of buspirone and DPAT on sexual behavior
 in the male rat may be possible at different parts of the central nervous
 system.
 If a tentative shared target site by DPAT and buspirone is the 5-HT1A
 receptor, than the same 5-HT receptor sub-type at different locations
 (brain, raphe nuclei, spinal cord and autonomic ganglia) may
 modulate rat sexual behavior in opposing ways.
 IT 21102-95-4, RMY-7378
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BIOL (Biological study)
 (modification of sexual behavior of Long-Evans male rats by drugs
 acting on the 5-HT1A receptor)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

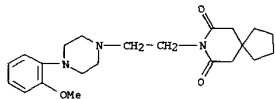


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REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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L14 ANSWER 73 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:120349 CAPLUS
 DOCUMENT NUMBER: 130:277169
 TITLE: Modulation of basal intracellular calcium by
 inverse agonists and phorbol myristate acetate in rat-1
 fibroblasts stably expressing .alpha.-ld-adrenoceptors
 AUTHOR(S): Garcia-Sainz, J. Adolfo; Torres-Padilla, Maria
 Elena
 CORPORATE SOURCE: Instituto de Fisiologia Celular, Universidad
 Nacional autonoma de Mexico, Mexico City, 04510, Mex.
 SOURCE: FEBS Letters (1999), 443(3), 277-281
 CODEN: FEBLAL; ISSN: 0014-5793
 PUBLISHER: Elsevier Science B.V.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In rat-1 fibroblasts stably expressing .alpha.-ld-adrenoceptors, RMY
 7378, phentolamine, chloroethylclonidine and 5-methylurapidil decreased
 basal [Ca2+]i. WB 4101 induced a very small effect on this parameter but
 when added before the other antagonists it blocked their effect. All these
 agents inhibited the action of norepinephrine. Phorbol myristate
 acetate also blocked the effect of norepinephrine and decreased basal [Ca2+]i.
 Staurosporine inhibited these effects of the phorbol ester. Our
 results suggest that: (1) .alpha.-ld-adrenoceptors exhibit spontaneous
 ligand-independent activity, (2) RMY 7378, phentolamine,
 chloroethylclonidine and 5-methylurapidil act as inverse agonists and
 (3) protein kinase C activation blocks spontaneous and agonist-stimulated
 .alpha.-ld-adrenoceptor activity.
 IT 21102-95-4, RMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BIOL (Biological study)
 (inverse agonist and protein kinase C modulation of intracellular
 calcium in rat-1 fibroblasts stably expressing .alpha.-ld-adrenoceptors)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

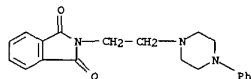
L14 ANSWER 73 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



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REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 74 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:68279 CAPLUS
 DOCUMENT NUMBER: 130:291449
 TITLE: Affinity for both 5-HT1A- and D1-receptors and
 anxiolytic activity of N-(arylpiperazinylalkyl)-
 phthalimides
 AUTHOR(S): Andronati, S. A.; Voronina, T. A.; Sava, V. M.;
 Molodavkin, G. M.; Hakan, S. Yu.; Soboleva, S. G.
 CORPORATE SOURCE: A.V. Bogatsky Physico-Chemical Institute, National
 Academy of Sciences of Ukraine, Odessa, 270080,
 Ukraine
 SOURCE: Molecular Recognition and Inclusion, Proceedings
 of the International Symposium on Molecular
 Recognition and Inclusion, 9th, Lyon, Sept. 7-12, 1996 (1998),
 Meeting Date 1996, 245-249. Editor(s): Coleman,
 Annette W. Kluwer: Dordrecht, Neth.
 CODEN: 67FSAY
 CONFERENCE
 DOCUMENT TYPE: English
 LANGUAGE: English
 AB The authors report here affinity for both 5-HT1A- and D1-receptors and
 anxiolytic activity of N-(arylpiperazinylalkyl)-phthalimides.
 IT 75000-24-7
 RL: BAC (Biological activity or effector, except adverse); RPR
 (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL
 (Biological study); PROC (Process)
 (affinity for both 5-HT1A- and D1-receptors and anxiolytic
 activity of N-(arylpiperazinylalkyl)-phthalimides)
 RN 75000-24-7 CAPLUS
 CN 1H-Indole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI)
 (CA INDEX NAME)

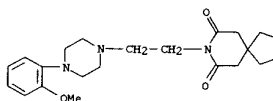


REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR
 THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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L14 ANSWER 75 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:55960 CAPLUS
 DOCUMENT NUMBER: 130:262474
 TITLE: Ultrasonic vocalizations in rat pups: effects of serotonergic ligands
 AUTHOR(S): Olivier, B.; Molensijk, H. E.; Van Der Heyden, J. A.
 Miczek, K.
 CORPORATE SOURCE: Department of CNS Pharmacology, Solvay Pharmaceuticals, Weesp, 1380 DA, Neth.
 SOURCE: Neuroscience and Biobehavioral Reviews (1998), 23(2), 215-227
 CODEN: NBREDE; ISSN: 0149-7634
 PUBLISHER: Elsevier Science Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Ligands with varying intrinsic activity and selectivity for the various subtypes of the serotonin receptor were tested in the rat pup ultrasonic vocalization (USV) model, a putative animal model reflecting anxiety. USV were elicited by isolating rat pups from their mother and littermates by placing them on a warm (37.degree.) or a cold (18.degree.) plate. Concurrently, the neg. geotaxis (NG) response and rectal temp. were detd. to assess the potentially sedative and hypothermic effects of putative anxiolytics. USV were reduced at low doses and in both temp. conditions by the full 5-HT1A receptor agonists flesinoxan and 8-OH-DPAT-HBR and the partial 5-HT1A receptor agonists buspirone, ipsapirone and BMY 7378. The 5-HT1A receptor antagonists NAN-190, (+-)-WAY 100135, and (S)-UH-301 reduced USV at higher doses and only in one of both test conditions. The selective 5-HT1A receptor antagonist DU 125530 did not influence USV at the cold plate up to high doses, although concomitantly the neg. geotaxis was disturbed. The neg. geotaxis was impaired after all 5-HT1A receptor ligands, except BMY 7378 and (+-)-WAY 100135. Hypothermia coincided with USV-suppression, except for NAN-190 and (S)-UH-301. The USV-suppressing action of flesinoxan (3 mg/kg) could be antagonized by DU 125530, but not its NG effect. However, the hypothermia induced by flesinoxan was antagonized by DU 125530. USV were also suppressed by the 5-HT uptake inhibitors fluvoxamine (both warm and cold plate) and

L14 ANSWER 76 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:53147 CAPLUS
 DOCUMENT NUMBER: 130:247259
 TITLE: Characterization of 5-HT1A receptor functional coupling in cells expressing the human 5-HT1A receptor
 AUTHOR(S): Dunlop, John; Zhang, Yingxin; Smith, Deborah L.; Schachter, Lee E.
 CORPORATE SOURCE: Wyeth-Ayerst Research, CNS Disorders, Princeton, NJ, 08543, USA
 SOURCE: Journal of Pharmacological and Toxicological Methods (1998), 40(1), 47-55
 CODEN: JPTMEZ; ISSN: 1056-8719
 PUBLISHER: Elsevier Science Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The functional activity of a series of 5-HT1A receptor ligands has been evaluated in a cell line expressing the human 5-HT1A receptor (h5-HT1A .cntdot. CHO) using the agonist-stimulated increase in extracellular acidification rate, measured with the microphysiometer, as a functional assay. Both 5-CT and 8-OH-DPAT were potent agonists in stimulating an increase in extracellular acidification rate in h5-HT1A .cntdot. CHO cells with estd. EC50 values of 1.2 and 7.8 nM, resp. Addnl., these two 5-HT1A receptor agonists elicited a similar max. response. Concn.-dependent agonist activity was also obsd. in the presence of buspirone, ipsapirone, BMY 7378, NAN-190 and WAY 100135, and each of these compds. behaved as partial 5-HT1A receptor agonists. The selective 5-HT1A receptor antagonist WAY 100635 produced a potent (IC50, 2.3 nM) and complete block of the 8-OH-DPAT-stimulated response. An evaluation of the inhibitory activity of a series of 5-HT1A receptor antagonists produced the following rank order of potency: WAY 100635 > LY 206130 (IC50, 7.1 nM) > WAY 100135 (30.8 nM) > pindolol (76.2 nM) > (-)-UH-301 (92.8 nM). Parallel studies on the inhibition of forskolin-stimulated adenyl cyclase activity in h5-HT1A .cntdot. CHO cells revealed that agonist potencies were generally similar between the two functional assays and were in good agreement with the estd. 5-HT1A receptor binding affinities. However, the relative efficacies detd. for the partial agonists in the cAMP assay were substantially greater than those obsd. with the microphysiometer. Finally, antagonists were considerably weaker in the cAMP assay compared

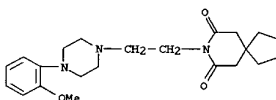
L14 ANSWER 75 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 clomipramine (only warm plate). The tricyclic antidepressant imipramine only decreased USV on the cold plate, however, in a U-shaped dose-response curve. At the highest dose tested, no decrease was present. The 5-HT uptake stimulant tianeptine reduced USV under both conditions. Fluvoxamine had no side effects, clomipramine induced hypothermia and tianeptine clearly had sedative properties. The 5-HT1B/2C receptor agonist TMPPP (trifluorometaphenylpiperazine) stimulated USV at a low dose at the cold plate and suppressed USV at a high dose under both conditions. The 5-HT2A/2C receptor antagonist Ketanserin enhanced USV at low doses under both conditions and had no effect at a higher dose. Concurrently heavy sedation and hypothermia occurred. The 5-HT3 receptor agonist phenylbiguanide and the 5-HT3 receptor antagonist ondansetron had no effect in this paradigm. Clearly, subtypes of the 5-HT receptor affect rat pup USV differentially.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (serotonin receptor subtype ligand differential effect on ultrasonic vocalization in rat pup)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



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REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS
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L14 ANSWER 76 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 with the microphysiometer. The evaluation of 5-HT1A ligands using the microphysiometer, which represents a very distinct indice of 5-HT1A receptor function compared with the cAMP assay, results in a different profile of functional activity.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (5-HT1A receptor functional coupling characterization in cells expressing the human 5-HT1A receptor as assessed by extracellular acidification rate detn. with the cytosensor microphysiometer and cAMP formation)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

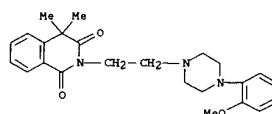


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REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS
 FORMAT RECORD. ALL CITATIONS AVAILABLE IN THE RE

L14 ANSWER 77 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:32567 CAPLUS
 DOCUMENT NUMBER: 130:76506
 TITLE: Role of the third intracellular loop of the
 alpha-2
 density
 AUTHOR(S): Heck, Donald A.; Bylund, David B.
 CORPORATE SOURCE: Dep. Pharmacology, Medical Center, Univ.
 Nebraska,
 SOURCE: Omaha, NE, 68198, USA
 10(2),
 101-110
 CODEN: PHRCF6
 PUBLISHER: Harwood Academic Publishers
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB It was previously shown that the mechanism of down-regulation of
 .alpha.-2
 adrenergic receptor subtypes is an increase in the rate const. for
 receptor disappearance. In addn., subtype-specific differences were
 found
 in the regulation of receptor d. in the presence of norepinephrine.
 For
 example, blocking functional G protein coupling with pertussis toxin
 alters the time-course of norepinephrine-induced down-regulation for
 .alpha.-2A receptors while having little effect on the time-course of
 receptor down-regulation for .alpha.-2B receptors. In contrast,
 treatment
 with pertussis toxin alone decreases .alpha.-2B receptor d. while
 having
 little effect on .alpha.-2A receptor d. To explore these
 subtype-specific
 differences, a chimeric receptor was constructed in which the 3rd
 intracellular loop of the .alpha.-2B receptor was replaced with the
 3rd
 intracellular loop of the .alpha.-2A receptor. It was found that the
 chimeric receptor exhibits similar characteristics to the wild-type
 receptor in terms of radioligand binding, potency of norepinephrine
 to
 down-regulate receptor d., and effects of pertussis toxin on
 receptor d.
 In contrast, replacement of the 3rd intracellular loop of the
 .alpha.-2B
 receptor with that of the .alpha.-2A receptor alters the regulation
 of
 receptor d. in both the absence and presence of norepinephrine.
 IT 67339-62-2, ARC-239
 RI: RAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); BIOL (Biological study)
 (affinity for .alpha.-2 adrenergic receptors and chimeric
 receptor)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

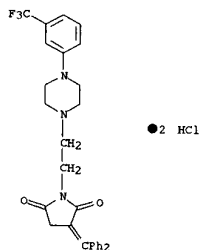
L14 ANSWER 77 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



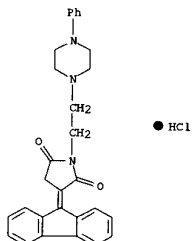
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR
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 RECORD. ALL CITATIONS AVAILABLE IN THE RE
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L14 ANSWER 78 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:04830 CAPLUS
 DOCUMENT NUMBER: 130:191412
 TITLE: Synthesis and Structure-Activity Relationships
 of a
 New Model of Arylpiperazines. 4.1-[.omega.-(4-
 Arylpiperazin-1-yl)alkyl]-3-(diphenylmethylene)-2,5-
 pyrrolidinediones and
 -3-(9H-fluoren-9-ylidene)-
 2,5-pyrrolidinediones: Study of the Steric
 Requirements of the Terminal Amide Fragment on
 5-HT1A
 Affinity/Selectivity
 AUTHOR(S): Lopez-Rodriguez, Maria L.; Morcillo, M. Jose;
 Rovat,
 Tandu X.; Fernandez, Esther; Vicente, Bruno;
 Sanz,
 Antonio M.; Hernandez, Medardo; Orensanz, Luis
 CORPORATE SOURCE: Departamento de Quimica Organica I Facultad de
 Ciencias Quimicas, Universidad Complutense,
 Madrid,
 28040, Spain
 SOURCE: Journal of Medicinal Chemistry (1999), 42(1),
 36-49
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 130:191412
 AB In the present paper, the authors report the synthesis and the
 binding
 profile on 5-HT1A, .alpha.1 and D2 receptors of a new series of
 1-[.omega.-(4-arylpiperazin-1-yl)alkyl]-3-(diphenylmethylene)-2,5-
 pyrrolidinediones (I) (1-4) and -3-(9H-fluoren-9-ylidene)-2,5-
 pyrrolidinediones (II) (1-4), in which the alkyl linker contains 1-4
 methylenes and the aryl group is variously substituted. The results
 obtained are compared to those previously reported for
 bicyclohydantoin
 and the related bicyclic amine series. A considerable part of the
 tested
 compds. demonstrated moderate to high affinity for 5-HT1A and
 .alpha.1
 receptor binding sites but had no affinity for D2 receptors. The
 study
 of the length of the alkyl chain and the imide substructure has allowed
 the
 authors to suggest some differences between the 5-HT1A and the
 .alpha.1-adrenergic receptors: (i) for I and II, affinity for the
 5-HT1A
 receptor as a function of the length of the methylene linker
 decreases in
 the order 4>1 .mchgt. 3.apprx.2, while for the .alpha.1 receptor
 affinity
 decreases in the order 3.apprx.4 > 1.apprx.2; (ii) the
 no-pharmacophoric
 steric pocket (receptor zone which does not hold the pharmacophore
 of the

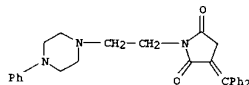
L14 ANSWER 78 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 ligand but holds a nonessential fragment of the mol.) in the 5-HT1A
 receptor has less restriction than the corresponding pocket in the
 .alpha.1 receptor. Compds. which are highly selective for
 .alpha.1-adrenergic receptors displayed antagonist activity. The best
 compromise between affinity and selectivity for 5-HT1A receptors is
 reached in these new series with n = 1, which is in agreement with the
 authors previous results for the bicyclohydantoin derivs. Two
 selected
 compds. retain agonist properties at postsynaptic 5-HT1A receptors.
 The
 same 5-HT1A agonist profile found in these compds. suggests the
 existence
 of two different no-pharmacophoric steric pockets in this receptor
 and a
 different interaction of compds. with n = 1 and n = 4. The
 information
 obtained from the interpretation of the energy minimization and
 2D-NOESY
 expts. of these compds. together with the synthesis and binding data
 of
 new conformationally restrained analogs is in good agreement with this
 working hypothesis.
 IT 220798-79-8P
 RI: BPR (Biological process); BSU (Biological study, unclassified);
 PRP
 (Properties); SPN (Synthetic preparation); BIOL (Biological study);
 PREP
 (Preparation); PROC (Process)
 (synthesis and structure-activity relationships of a new model of
 arylpiperazines and study of steric requirements of terminal amide
 fragment on 5-HT1A affinity/selectivity in relation to
 .alpha.1-adrenergic and D2 receptors)
 RN 220798-79-8 CAPLUS
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-[4-(3-
 (trifluoromethyl)phenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI)
 (CA
 INDEX NAME)



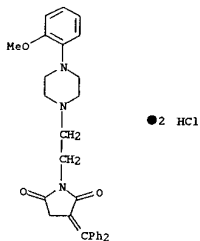
IT 193287-12-6P 193287-13-7P 193287-15-9P
 193287-16-0P 193287-18-2P 193287-19-3P
 220798-76-5P 220798-85-6P 220798-90-3P
 RL: BPR (Biological process); BSU (Biological study, unclassified);
 SPN (Synthetic preparation); BIOL (Biological study); PREP
 (Preparation); PROC
 (Process)
 (synthesis and structure-activity relationships of a new model of
 arylpiperazines and study of steric requirements of terminal amide
 fragment on 5-HT1A affinity/selectivity in relation to
 .alpha.1-adrenergic and D2 receptors)
 RN 193287-12-6 CAPLUS
 CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-(4-phenyl-1-
 piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



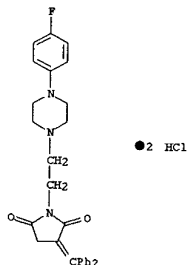
RN 193287-13-7 CAPLUS
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-phenyl-1-
 piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



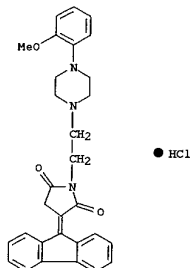
RN 193287-15-9 CAPLUS
 CN 2,5-Pyrrolidinedione,
 3-(diphenylmethylene)-1-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



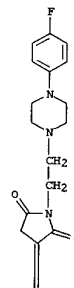
RN 193287-16-0 CAPLUS
 CN 2,5-Pyrrolidinedione,
 3-(diphenylmethylene)-1-[2-[4-(4-fluorophenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



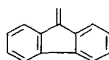
RN 193287-18-2 CAPLUS
 CN 2,5-Pyrrolidinedione,
 3-(9H-fluoren-9-ylidene)-1-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



RN 193287-19-3 CAPLUS
 CN 2,5-Pyrrolidinedione,
 3-(9H-fluoren-9-ylidene)-1-[2-[4-(4-fluorophenyl)-1-
 piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

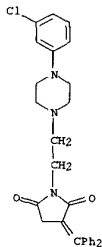


PAGE 2-A



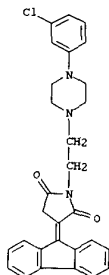
● HCl

RN 220798-76-5 CAPLUS
 CN 2,5-Pyrrolidinedione,
 1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-3-(
 (diphenylmethylene)-, dihydrochloride (9CI) (CA INDEX NAME)



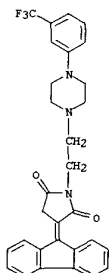
● 2 HCl

RN 220798-85-6 CAPLUS
 CN 2,5-Pyrrolidinedione,
 1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-3-(9H-
 fluoren-9-ylidene)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 220798-90-3 CAPLUS
 CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-[4-[3-(
 (trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride
 (9CI) (CA INDEX NAME)

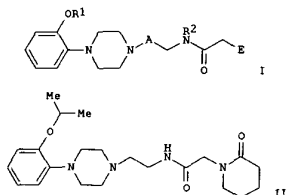


● HCl

REFERENCE COUNT: 48 THERE ARE 48 CITED REFERENCES AVAILABLE FOR THIS

L14 ANSWER 79 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:764277 CAPLUS
 DOCUMENT NUMBER: 130:24968
 TITLE: Preparation of aryl-substituted piperazines
 useful in
 the treatment of benign prostatic hyperplasia
 Jolliffe, Linda; Murray, William; Pulito,
 Virginia;
 Reitz, Alan; Li, Xiaobing; Mulcahy, Linda;
 Maryanoff,
 Cynthia; Villani, Frank
 PATENT ASSIGNEE(S): Ortho-McNeil Pharmaceutical Inc., USA
 SOURCE: PCT Int. Appl., 38 pp.
 CODEN: FIXX02
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

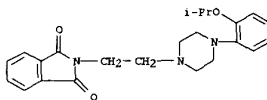
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|---|-----------------|-------------|
| WO 9851298 | A1 | 19981119 | WO 1998-US9023 | 19980508 |
| DE, | W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, | | |
| KZ, | | DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, | | |
| PL, | | LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, | | |
| UZ, | | PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, | | |
| ES, | | VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | |
| CI, | RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, | | |
| | | FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, | | |
| | | CM, GA, GN, ML, MR, NE, SN, TD, TG | | |
| AU 9873669 | A1 | 19981208 | AU 1998-73669 | 19980508 |
| EP 984777 | A1 | 20000315 | EP 1998-920950 | 19980508 |
| PT, | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, | | |
| | | IE, FI, RO | | |
| US 6071915 | A | 20000606 | US 1998-74789 | 19980508 |
| BR 9809804 | A | 20000627 | BR 1998-9804 | 19980508 |
| JP 2802511065 | T2 | 20000409 | JP 1998-549276 | 19980508 |
| ZA 9803968 | A | 19991111 | ZA 1998-3968 | 19980511 |
| NO 9905518 | A | 20000111 | NO 1999-5518 | 19991111 |
| US 6303594 | B1 | 20011016 | US 2000-526224 | 20000315 |
| PRIORITY APPLM. INFO.: | | | US 1997-462369 | P 19970512 |
| | | | US 1998-74789 | A1 19980508 |
| | | | WO 1998-US9023 | W 19980508 |
| OTHER SOURCE(S): | | MARPAT 130:24968 | | |
| GI | | | | |



AB The title compds. (I; A = (CH₂)_n; R₁ = H, C1-6 alkyl, (un)substituted Ph, substituted phenyl (C1-5 alkyl); R₂ = H, C1-6 alkyl, C1-5 alkenyl, C1-5 alkynyl, (un)substituted phenyl (C1-5 alkyl); E = piperidino, phthalimido, etc.; n = 1-6] and their pharmaceutically acceptable salts, .alpha.-1A adrenergic receptor antagonists useful for the therapy of benign prostatic hyperplasia, were prepd. Pharmaceutical compns. contg. I and intermediates used in their manuf. are also claimed. For example, hydrazinolysis of 1-(2-phthalimidoethyl)-4-(2-isopropoxyphenyl)piperazine with MeNH₂ gave 1-(2-aminoethyl)-4-[2-(2-isopropoxyphenyl)piperazine which was amidated with 1-carboxymethyl-2-piperidone (prepn. by N-alkylation of .delta.-valerolactone with BrCH₂CO₂Me₃ followed by ester hydrolysis given) to give II. This (as citrate salt) had IC₅₀ 8.7 nmol for binding on .alpha._{1A} receptor subtype cloned with poly(A)⁺ RNA from human hippocampus and prostate tissue.

IT 216252-67-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and hydrazinolysis; prepn. of aryl-substituted piperazines as .alpha.-1A adrenoceptor antagonists for therapy of benign prostatic hyperplasia)

RN 216252-67-4 CAPLUS
 CN 1H-Isindole-1,3(2H)-dione, 2-[2-[4-[2-(1-methylethoxy)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



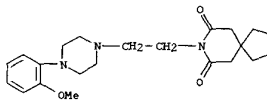
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RECORD.

FORMAT

ACCESSION NUMBER: 1998:727766 CAPLUS
 DOCUMENT NUMBER: 130:90774
 TITLE: .alpha._{1D}-Adrenoceptors contribute to the neurogenic vasopressor response in pithed rats
 AUTHOR(S): Rodriguez-Silverio, J.; Castillo, E. F.; Lopez, R. M.; Robadilla, R. A.; Castillo, C.
 CORPORATE SOURCE: Seccion de Estudios de Posgrado e Investigacion, Escuela Superior de Medicina del IPN, Plan de San Luis y Diaz Miron, Casco de Sto Tomas, Mexico, 17, Mex. SOURCE: Fundamental & Clinical Pharmacology (1998), 12(6), 584-589
 PUBLISHER: CODEN: FCPHEZ; ISSN: 0767-3981
 DOCUMENT TYPE: Editions Scientifiques et Medicales Elsevier
 LANGUAGE: Journal English
 AB The aim of the present study was to assess the role of vascular .alpha._{1D}-adrenoceptors in the sympathetic vasopressor response in vivo. Specifically, we evaluated the effect of a selective .alpha._{1D}-adrenoceptor antagonist, BMY 7378 (8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-8-azaspiro[4.5]decane-7,9-dione 2HCl), on the vasopressor response induced by preganglionic (T7-T9) sympathetic stimulation in the pithed rat. The vasopressor response was dose-dependently sensitive to inhibition by i.v. BMY 7378 (0.1, 0.31, 1 and 3.1 mg/kg), doses of 1 and 3.1 mg/kg being equally effective. Like BMY 7378, 5-methylurapidil (0.1, 0.31, 1 and 3.1 mg/kg) antagonized the vasopressor response to spinal stimulation; doses of 1 and 3.1 mg/kg were also equally effective. In combination expts., BMY 7378 (1 mg/kg, i.v.) and the .alpha._{1A}-adrenoceptor antagonist, 5-methylurapidil (1 mg/kg, i.v.), showed an additive effect. The present results demonstrate that the .alpha._{1D}-adrenoceptor subtype plays an important role in the pressor response to sympathetic nerve stimulation in the pithed rat, and confirm the participation of the .alpha._{1A}-adrenoceptor subtype in the same response.

IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (.alpha._{1D}-adrenoceptors contribute to the neurogenic vasopressor response in pithed rats)

RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

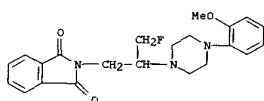


● 2 HCl

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RECORD.

FORMAT

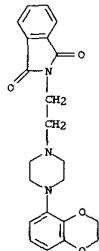
L14 ANSWER 81 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:713718 CAPLUS
 DOCUMENT NUMBER: 130:52388
 TITLE: Studies on quinazoline IX. Fluorination versus 1,2-migration in the reaction of 1,3-bifunctionalized amino-2-propanol with DAST
 AUTHOR(S): Chern, Yi-Wang; Chang, Jun-Yi; Usifoh, Cyril O.; Gutsait, Alexander
 CORPORATE SOURCE: Sch. Pharmacy, Coll. Medicine, National Taiwan Univ., Taipei, Taiwan
 SOURCE: Tetrahedron Letters (1998), 39(46), 8483-8486
 CODEN: TELEAY; ISSN: 0040-4039
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 130:52388
 AB Treatment of 1-phthaloylamino-3-[4-(2-methoxyphenyl)piperazin-1-yl]propanol with diethylaminosulfur trifluoride (DAST) induced 1,2-migration via a proposed spiroaziridinium intermediate to give N-[2-fluoro-3-[4-(2-methoxyphenyl)piperazin-1-yl]propyl]phthalimide in 13% yield and N-[2-fluoromethyl-2-[4-(2-methoxyphenyl)piperazin-1-yl]ethyl]phthalimide in 73% yield.
 IT 217170-74-6P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (fluorination vs. 1,2-migration in reaction of 1,3-bifunctionalized amino-2-propanol with DAST)
 RN 217170-74-6 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[3-fluoro-2-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]- (SCI) (CA INDEX NAME)



REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 82 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:660055 CAPLUS
 DOCUMENT NUMBER: 130:3828
 TITLE: Functional characteristics of a series of N4-substituted 1-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazines as 5-HT1A receptor ligands. Structure-activity relationships
 AUTHOR(S): Van Steen, B. J.; Van Wijngaarden, L.; Ronken, E.; Soudijn, W.
 CORPORATE SOURCE: Solvay Pharmaceuticals Research Laboratories, Weesp, 1380, Neth.
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(18), 2457-2462
 CODEN: BMCLES; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The agonistic/antagonistic profile of a series of 10 N4-substituted 1-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazines is evaluated in the in vitro adenyl cyclase assay. The profile is severely affected by the characteristics of the N4-substituents ranging from full agonism (benzamidodethyl deriv.), mixed agonism/antagonism (phthalimidoethyl deriv.) to predominantly antagonism (saccharinbutyl derivative). A novel full antagonist, as potent as WAY 100635, is obtained by substitution of Cl at C-7 of the benzodioxinyl moiety in the saccharinbutyl derivative.
 IT 171877-07-9P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 as (structure-activity relationship of of (benzodioxinyl)piperazines as 5-HT1A receptor ligands)
 RN 171877-07-9 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]- (SCI) (CA INDEX NAME)

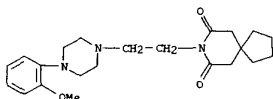
L14 ANSWER 82 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L14 ANSWER 83 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:508546 CAPLUS
 DOCUMENT NUMBER: 129:211986
 TITLE: .alpha.1L-adrenoceptors in canine pulmonary artery
 AUTHOR(S): Flavahan, N. A.; Hales, M. A.; Aleksoitch, T. D.; Gaine, S. P.; Vanhouts, P. M.
 CORPORATE SOURCE: Department of Medicine, Johns Hopkins University, Baltimore, MD, USA
 SOURCE: Journal of Cardiovascular Pharmacology (1998), 32(2), 308-316
 CODEN: JCPCDT; ISSN: 0160-2446
 PUBLISHER: Lippincott-Raven Publishers
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The aim of this study was to characterize the .alpha.1-adrenoceptors of the canine pulmonary artery. Arterial rings from lower lung lobes were suspended for isometric-tension recording in the presence of cocaine (5 .times. 10-6 M), hydrocortisone (3 .times. 10-5 M), propranolol (5 .times. 10-6 M), and rauwolfscine (10-7 M) to inhibit neuronal uptake, extraneuronal uptake, and .beta.- and .alpha.2-adrenoceptors, resp. Prazosin was more potent against contractions evoked by phenylephrine (pA2 of 9.7) compared with methoxamine (pA2 of 8.4). SZL49 (10-8 and 3 .times. 10-8 M), an irreversible .alpha.1-adrenergic antagonist, inhibited responses to phenylephrine but not methoxamine. With norepinephrine, low concns. of prazosin (3 .times. 10-10 M and 10-9 M) caused inhibition of the concn.-response curve; a higher concn. (3 .times. 10-9 M) failed to produce further inhibition, whereas increasing the concn. of the antagonist (to 10-8 and 3 .times. 10-8 M) caused further rightward shifts in the concn.-response curve. The Arunlakshana and Schild plot revealed two components corresponding to pA2 values of 9.8 and 8.4. After SZL49 (3 .times. 10-8 M), the Arunlakshana and Schild plot for the interaction between norepinephrine and prazosin was linear and generated a pA2 of 8.3. Contractions evoked by phenylephrine were inhibited by the .alpha.1B/.alpha.1D-adrenoceptor antagonist, chloroethylclonidine (10-5 M), or by the .alpha.1B-antagonist, risperidone (pA2 value of 8.5), but were relatively resistant to inhibition by the selective .alpha.1D-antagonist, RMY7378 (-log KB of 6.1). The results suggest that two .alpha.1-adrenoceptor subtypes mediate contraction of the canine pulmonary artery. One subtype has high affinity for prazosin (.alpha.1H,

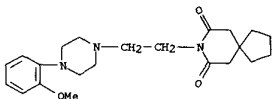
L14 ANSWER 83 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
likely to be .alpha.1B), is activated by phenylephrine, and is inhibited by SZL49. The other subtype has lower affinity for prazosin (.alpha.1L), is stimulated by methoxamine, and is relatively resistant to SZL49. The physiol. agonist, norepinephrine, causes contraction by activating both subtypes.
IT 21102-95-4, BMY7378
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BVU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L14 ANSWER 84 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:401962 CAPLUS
DOCUMENT NUMBER: 129:130877
TITLE: Search for .alpha.1-adrenoceptor subtypes
selective antagonists: design, synthesis and biological activity of cystazosin, an .alpha.1D-adrenoceptor antagonist
AUTHOR(S): Minarini, Anna; Budriesi, Roberto; Chiarini, Alberto;
CORPORATE SOURCE: Leonardi, Amedeo; Melchiorre, Carlo
Department of Pharmaceutical Sciences, University of Bologna, Bologna, I-40126, Italy
SOURCE: Bioorganic & Medicinal Chemistry Letters (1998), 8(11), 1353-1358
CODEN: BMCLER; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:130877
AB Two novel quinazolines related to both prazosin and its open analog were synthesized, and their biol. profile at .alpha.1-adrenoceptor subtypes was assessed by functional assays in rat isolated tissues, namely prostatic vas deferens (.alpha.1A), spleen (.alpha.1B) and aorta (.alpha.1D). Furthermore, the binding profile of cystazosin was assessed at native .alpha.2 and D2 receptors, and cloned human 5-HT1A receptors, in comparison to prazosin, (+)-cylazosin, the prazosin open analog and BMY 7383. It turned out that the cystamine-bearing quinazoline (cystazosin) has a reversed affinity profile relative to (+)-cylazosin owing to a higher affinity for .alpha.1D-adrenoceptors and a significantly lower affinity for the .alpha.1A and .alpha.1B subtypes. Furthermore, in comparison to BMY 7378, cystazosin displays a much better specificity profile since it has lower affinity for D2 and 5-HT1A receptors.
IT 21102-95-4, BMY 7378
RL: BAC (Biological activity or effector, except adverse); BPR (Biological Process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
PROC (Process) (search for .alpha.1-adrenoceptor subtype-selective antagonists by design and synthesis and biol. activity of cystazosin)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 84 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

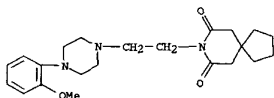


● 2 HCl

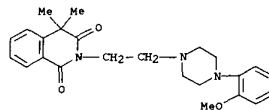
L14 ANSWER 85 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:386654 CAPLUS
DOCUMENT NUMBER: 129:131120
TITLE: Effects of imidazoline derivatives on cholinergic motility in guinea-pig ileum: involvement of presynaptic .alpha.2-adrenoceptors or imidazoline receptors?
AUTHOR(S): Colucci, Rocchina; Blandizzi, Corrado; Carignani, Diego; Placanica, Giorgio; Lazzeri, Gloria; Del Tacca, Mario
CORPORATE SOURCE: Department of Oncology, Division of Pharmacology and Chemotherapy, University of Pisa, Via Roma 55, I-56126, Italy
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1998), 357(6), 682-691
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study investigates the possibility that imidazoline receptors mediate modulation of cholinergic motor functions of the guinea-pig ileum. For this purpose, the effects of a series of compds. with known affinity for .alpha.2-adrenoceptors and/or imidazoline recognition sites were examd. on the cholinergic twitch contractions evoked by elec. field stimulation (0.1 Hz) of longitudinal muscle-myenteric plexus preps. Addnl. expts. were carried out on ileal strips preincubated with [³H]choline, superfused with physiol. salt soln. contg. hemicholinium-3, and subjected to elec. field stimulation (1 Hz). The stimulation-induced outflow of radioactivity was taken as an index of endogenous acetylcholine release. .alpha.-Methyl-noradrenaline, noradrenaline, clonidine, medetomidine, oxymetazoline and xylazine caused a concn.-dependent inhibition of twitch responses (IC50 from 0.13 to 1.05 .mu.M; Emax from 85.9 to 92.5%). Rilménidine and agmatine were less potent in reducing the twitch activity, and the latter compd. acted also with low intrinsic activity (IC50=44.9 .mu.M; Emax=35.5%). In interaction expts., the inhibitory action of clonidine on twitch responses was competitively antagonized by RX 821002 [2-(2-methoxy-1,4-benzodioxan-2-yl)-2-imidazoline], idazoxan, rauwolfscine, yohimbine and BRL 4408
[2-[2H-(1-methyl-1,3-dihydroisoindole)-methyl]-4,5-dihydroimidazoline], whereas prazosin (10 .mu.M), ARC 239
[2-(2,4-[o-methoxyphenyl]-piperazin-1-yl)ethyl]-4,4-dimethyl-1,3-(2H,4H)-isoquinolindione, 10 .mu.M] and BRL 41992 [1,2-dimethyl-2,3,9,13b-tetrahydro-1H-dibenz[c,f]imidazol[1,5-a]azepine; 10 .mu.M] were without effect. Rauwolfscine antagonized the

L14 ANSWER 85 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
inhibitory effects of various agonists on ileal twitch activity in a competitive manner and with similar potency. Agmatine and idazoxan did not significantly modify the twitch contractions when tested in the presence of .alpha.2-adrenoceptor blockade by rauwolscine (3 .mu.M) or RX 821002 (1 .mu.M). Linear regression anal. showed that the affinity values of antagonists correlated with their affinity at the .alpha.2A and .alpha.2D binding sites as well as at previously classified .alpha.2A/Dadrenoceptor subtypes, whereas no significant correlation was obtained when comparing the potency ests. of agonists and antagonists with the affinity at I1 or I2 binding sites. When tested on the elec. induced outflow of tritium, .alpha.-methyl-noradrenaline, noradrenaline, clonidine, medetomidine, oxymetazoline, xylazine and rilmenidine yielded inhibitory concn.-response curves which were shifted rightward to a similar extent in the presence of rauwolscine (3 .mu.M). In the absence of further drugs, agmatine significantly reduced the evoked tritium outflow at the highest concns. tested (10 and 100 .mu.M), whereas idazoxan (up to 100 .mu.M) was without effect. When RX 821002 (1 .mu.M) was added to the superfusion medium, neither agmatine nor idazoxan modified the evoked outflow of radioactivity. The results argue against modulation by imidazoline receptors of acetylcholine release from myenteric plexus nerve terminals. They provide evidence that compds. endowed with imidazoline-like structures affect the cholinergic motor activity of the guinea-pig ileum by interacting with presynaptic .alpha.2-adrenoceptors belonging to the .alpha.2D subtype.
IT 67339-62-2, AR-C 239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (imidazoline deriv. effect on cholinergic motility in guinea-pig ileum in relation to involvement of presynaptic .alpha.2-adrenoceptors or imidazoline receptors)
RN 67339-62-2 CAPLUS
CN 1,3-(2H,4H)-[isquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

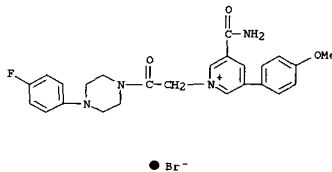
L14 ANSWER 86 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:349268 CAPLUS
DOCUMENT NUMBER: 129:81649
TITLE: Theoretical descriptors in quantitative structure-affinity and selectivity relationship study
of potent N4-substituted arylpiperazine 5-HT1A receptor antagonists
AUTHOR(S): Menziani, M. C.; De Benedetti, P. G.; Karelson, M.
CORPORATE SOURCE: Dipartimento di Chimica, Universita' di Modena, Modena, 41100, Italy
SOURCE: Bioorganic & Medicinal Chemistry (1998), 6(5), 535-550
CODEN: RMECEP; ISSN: 0968-0896
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The ability of ad hoc defined size and shape descriptors and theor. descriptors derived on a single structure to give powerful interpretative and predictive QSAR models was compared and evaluated with respect to the quality of the pharmacol. data available for structurally diverse 5-HT1A receptor antagonists, displaying selectivity towards the .alpha.1-adrenergic receptor.
IT 21102-94-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); CAT (Catalyst use); PEF (Physical, engineering or chemical process); PRC (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (theor. descriptors in QSAR study of arylpiperazine 5-HT1A receptor antagonists)
RN 21102-94-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 85 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 87 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:348051 CAPLUS
DOCUMENT NUMBER: 129:81649
TITLE: Solid phase synthesis of a 1,3,5-trisubstituted pyridinium salt library
AUTHOR(S): Pradiip
CORPORATE SOURCE: Medicinal Chemistry Department, SmithKline Beecham Pharmaceuticals, Colleville, PA, 19426-0989, USA
SOURCE: Tetrahedron Letters (1998), 39(23), 3885-3888
CODEN: TELEAY; ISSN: 0040-4039
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 129:81649
AB The synthesis of a 1,3,5-trisubstituted pyridinium salt combinatorial array contg. two variable groups was accomplished in good yields.
This entailed the incorporation of 5-bromonicotinic acid onto the resin, followed by Pd(0) catalyzed Suzuki coupling, then alkylation of the pyridine nitrogen and finally cleavage from the resin. A mix and split scheme was also carried out.
IT 209398-54-9P
RL: SPN (Synthetic preparation); PREP (Preparation) (solid phase synthesis of a trisubstituted pyridinium salt library)
RN 209398-54-9 CAPLUS
CN Pyridinium, 3-[aminocarbonyl]-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]-2-oxoethyl]-5-[4-methoxyphenyl]-, bromide (9CI) (CA INDEX NAME)



L14 ANSWER 88 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:319424 CAPLUS
 DOCUMENT NUMBER: 129:63374
 TITLE: Pharmacological and immunocytochemical characterization of subtypes of alpha-1 adrenoceptors

in dog aorta
 AUTHOR(S): Low, A. M.; Lu-Chao, H.; Wang, Y. F.; Brown, R. D.; Kwan, C. Y.; Daniel, E. E.
 CORPORATE SOURCE: Department of Biomedical Sciences, McMaster University, Hamilton, ON, L8N 3Z5, Can.
 SOURCE: Journal of Pharmacology and Experimental Therapeutics
 (1998), 285(2), 894-901
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: Williams & Wilkins
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB In this study, the effects of nine alpha-1 adrenoceptor antagonists (prazosin, WB 4101 (WB), chloroethylclonidine (CEC), 5-methylurapidil (5-MU), RMY 7378 (RMY), MDL 73005EF (MDL73), MDL 72832 (MDL72), RS 17053 (RS) and SK&F 105854 (SKF)) were studied on contractile responses to phenylephrine (PE) of the endothelium-denuded dog aorta in vitro.

All antagonists, except CEC, 5-MU and RS, produced concn.-dependent competitive inhibition of contractile responses of the aorta to PE.

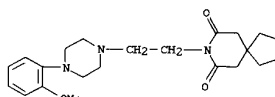
The rightward shift of the concn.-response curves of PE yielded const. pKB values with increasing antagonist concns. in most cases allowing a single pooled value to be detd.: for prazosin, a pKB of 8.99+-0.11 (n = 20, KB of 1.03 nM); for WB, a pKB of 8.75+-0.08 (n = 23, KB of 1.76 nM); for RMY, a pKB of 7.21+-0.13 (n = 13, KB of 62 nM); for MDL72, a pKB of 7.95+-0.15 (n = 12, KB of 11.2 nM); and for SK&F 105854, a pKB of 5.82+-0.08 (n = 15, KB of 1.52 .mu.M). For MDL73, pKB values decreased with antagonist concn.: 7.88+-0.06 at 10 nM, 7.56+-0.28 at 100 nM and 6.92+-0.18 at 1000 nM, which suggests the presence of more than one receptor subtype. CEC (10 and 100 .mu.M) almost completely inhibited responses to PE; lower concns. had no significant effect. 5-MU (10-300 nM) and RS (3-300 nM) were ineffective antagonists in this tissue.

Because WB, a highly selective alpha-1D and alpha-1A adrenoceptor subtypes inhibitor, blocked PE responses (with less affinity than for alpha-1A adrenoceptors), and 5-MU and RS, which are selective blockers for alpha-1A adrenoceptor, were ineffective, we conclude that alpha-1A adrenoceptors are absent in the dog aorta. The effects of the less selective MDL72 were

L14 ANSWER 88 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 inconsistent with actions at alpha-1B or alpha-1D adrenoceptors. Although WB shifted the PE concn.-response curve to the right, the abilities of RMY, MDL73 and SKF to inhibit competitively PE contraction were of lower affinity compared with expectations for interaction with alpha-1D adrenoceptors; they are not the predominant subtype. The complete inhibition of PE responses by CEC suggests that the dog aorta contains the alpha-1B adrenoceptor subtype. In immunocytochem. studies of the expression of alpha-1B adrenoceptor, all cells apparently expressed this protein. Moreover, Western blot studies of the microsomal fractions confirmed the presence of alpha-1B adrenoceptors. In the dog aorta, the alpha-1 adrenoceptors predominantly resemble alpha-1B rather than alpha-1D adrenoceptors as reported in the rat aorta.

IT 21102-95-4, RMY 7378
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (pharmacol. and immunocytochem. characterization of subtypes of alpha-1 adrenoceptors in dog aorta)

RN 21102-95-4 CAPLUS
 CN 8-AzaSpiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 89 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:304032 CAPLUS
 DOCUMENT NUMBER: 129:62431
 TITLE: Computer modeling of size and shape descriptors of .alpha.1-adrenergic receptor antagonists and quantitative structure-affinity/selectivity relationships

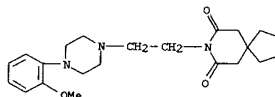
AUTHOR(S): Montorsi, Monica; Manziani, M. Cristina; Cocchi, Marina; Fanelli, Francesca; De Benedetti, Pier G.
 CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena, Modena, 41100, Italy
 SOURCE: Methods (Orlando, Florida) (1998), 14(3), 239-254
 CODEN: MTHDES; ISSN: 1046-2023
 PUBLISHER: Academic Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Computational chem. and mol. modeling procedures allow the authors to define and compute ad hoc size and shape descriptors on the different prototypic forms assumed by drugs in biotest solns. Together with exptl. data measured on a well-identified target receptor, these descriptors are essential elements for obtaining simple, consistent, comparable, and easily interpretable theor. quant. structure-activity relation (QSAR) models based on the ligand similarity-target receptor complementarity paradigm. In this context, quant. size and shape affinity/subtype selectivity relationships have been modeled for a large set of very heterogeneous .alpha.1a-, .alpha.1b-, and .alpha.1d- adrenergic receptor antagonists. The linear QSAR models generated have been validated by predicting both binding affinity and selectivity of a test set of noncongeneric antagonists. The satisfactory results obtained highlight both the simplicity and the versatility of the approach presented.

IT 21102-95-4, RMY 7378 67339-62-2, ARC 239
 99718-67-9
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (computer modeling of size and shape descriptors of .alpha.1-adrenergic receptor antagonists and quant. structure-affinity/selectivity relationships)

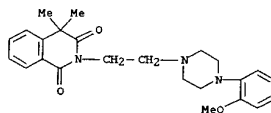
RN 21102-95-4 CAPLUS
 CN 8-AzaSpiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 89 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

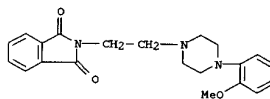


●2 HCl

RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

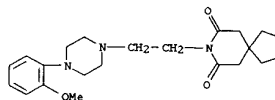


RN 99718-67-9 CAPLUS
 CN 1H-Indole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



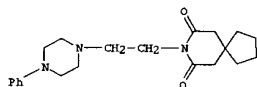
L14 ANSWER 90 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:285099 CAPLUS
 DOCUMENT NUMBER: 129:63311
 TITLE: Characterization of .alpha.1-adrenoceptor subtypes in the pig
 AUTHOR(S): Wikberg-Matasson, Anna; Wikberg, Jarl E. S.; Uhlen, Staffan
 CORPORATE SOURCE: Academic Hospital, Department of Ophthalmology, Uppsala University, Uppsala, Swed.
 SOURCE: European Journal of Pharmacology (1998), 347(2/3), 301-309
 PUBLISHER: CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Elsevier Science B.V.
 LANGUAGE: English
 AB The identities of the .alpha.1-adrenoceptor subtypes present in various tissues of the pig were studied using [3H]prazosin radioligand binding. The subtypes were characterized by performing competition expts. for various subtype selective drugs. In the cerebral cortex, spleen and heart, both .alpha.1A- and .alpha.1B-adrenoceptors were detected. In the liver was found only the .alpha.1A-subtype, while in the aorta was found only the .alpha.1B-subtype. An .alpha.1-adrenoceptor subtype was present in the adrenal gland with a high affinity for prazosin, the pKd value being 9.6, but with relatively low affinities for other .alpha.1-adrenoceptor binding drugs. The adrenal gland .alpha.1-adrenoceptor did not seem to represent the classical .alpha.1D-subtype, since drugs selective for the .alpha.1D-subtype in other species, including RMY7378 and SKF104856, showed low affinities for the pig adrenal gland .alpha.1-adrenoceptor.
 IT 21102-95-4, RMY 7378
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (.alpha.1-adrenoceptor subtypes characterization in pig organs)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 90 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

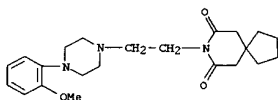


● 2 HCl

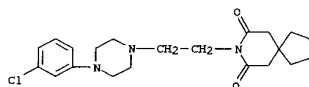
L14 ANSWER 91 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:254237 CAPLUS
 DOCUMENT NUMBER: 129:22916
 TITLE: Study of structure-activity relations in a series of buspirone analogs using an electron-topological approach
 AUTHOR(S): Dimoglo, A. S.; Chumakov, Yu. M.; Simonov, Yu. A.; Andronati, S. A.; Bocelli, G.
 CORPORATE SOURCE: Inst. Khim., AN Resp. Moldova, Chisinau, Moldova
 SOURCE: Khimiko-Farmatsevticheskii Zhurnal (1998), 32(1), 36-40
 CODEN: KHFZAN; ISSN: 0023-1134
 PUBLISHER: Izdatel'stvo Folium
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 AB The structure-related psychotropic activity of a series of buspirone analogs is described.
 IT 21090-07-3 21102-94-3 21103-20-8
 25024-93-5 25024-94-6 75000-28-1
 83928-69-2 83928-77-2 83928-78-3
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (structure-psychotropic activity relations in series of buspirone analogs: electron-topol. approach)
 RN 21090-07-3 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



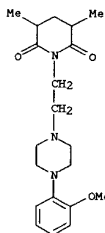
RN 21102-94-3 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



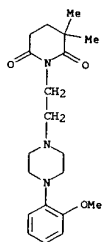
L14 ANSWER 91 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 21103-20-8 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



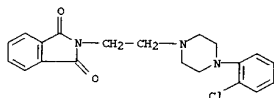
RN 25024-93-5 CAPLUS
 CN 2,6-Piperidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)



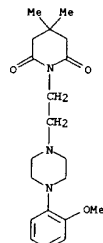
RN 25024-94-6 CAPLUS
 CN 2,6-Piperidinedione, 1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,3-dimethyl- (9CI) (CA INDEX NAME)



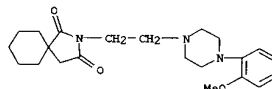
RN 75000-28-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione,
2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)



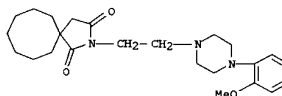
RN 83928-69-2 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-
dimethyl- (9CI) (CA INDEX NAME)



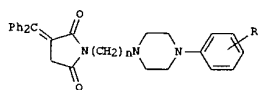
RN 83928-77-2 CAPLUS
CN 2-Azaspiro[4.5]decane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83928-78-3 CAPLUS
CN 2-Azaspiro[4.7]dodecane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

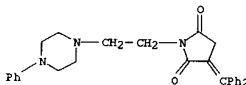


L14 ANSWER 92 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:220189 CAPLUS
DOCUMENT NUMBER: 128:308471
TITLE: 1-[omega-(4-Arylpiperazin-1-yl)alkyl]-3-diphenylmethylene-2,5-pyrrolidinediones as 5-HT1A receptor ligands: study of the steric requirements of the terminal amide fragment on 5-HT1A affinity/selectivity
AUTHOR(S): Lopez-Rodriguez, Maria L.; Morcillo, M. Jose;
Tandu K.; Fernandez, Esther; Sanz, Antonio M.; Orensanz, Luis
CORPORATE SOURCE: Department de Quimica Organica I, Fac. de Ciencias
SOURCES: Quimicas, Univ. Complutense, Madrid, 28040, Spain
Bioorganic & Medicinal Chemistry Letters (1998), 8(6), 581-586
CODEN: BMCLES; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

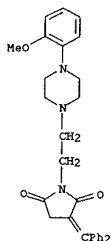


AB Title compds. I [n = 1-4; R = H, 2-OMe, 3-Cl, 3-CF3, 4-F] were
prepd. from the maleimide, CH2O, and the piperazine or from the maleic anhydride
and the aminoalkylpiperazine and their binding profiles for the 5-HT1A, .alpha.1, and D2 receptors were evaluated. The study of the length
of the alkyl chain and the imide substructure suggests some important
differences between the non-pharmacophoric sites of both 5-HT1A and .alpha.-adrenergic
receptors, which could be of great importance in designing new
selective ligands.
IT 206430-38-8P 206430-41-3P 206430-43-5P
206430-45-7P 206430-46-8P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological
study); PREP (Preparation)
(steric requirements of the terminal amide fragment of

L14 ANSWER 92 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
aryl piperazinylalkylpyrrolidinediones on 5-HT1A affinity/selectivity
RN 206430-38-8 CAPLUS
CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-phenyl-1-
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

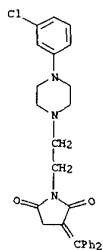


RN 206430-41-3 CAPLUS
CN 2,5-Pyrrolidinedione,
3-(diphenylmethylene)-1-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

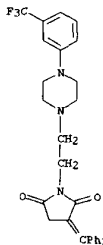


RN 206430-43-5 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-3-
(diphenylmethylene)- (9CI) (CA INDEX NAME)

L14 ANSWER 92 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

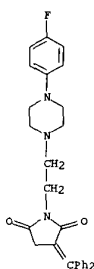


RN 206430-45-7 CAPLUS
CN 2,5-Pyrrolidinedione, 3-((diphenylmethylene)-1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



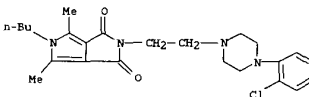
RN 206430-46-8 CAPLUS
CN 2,5-Pyrrolidinedione, 3-((diphenylmethylene)-1-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 92 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 93 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 5-butyl-2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)

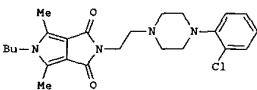


L14 ANSWER 93 OF 263 CAPLUS COPYRIGHT 2002 ACS

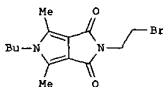
ACCESSION NUMBER: 1998:56192 CAPLUS
DOCUMENT NUMBER: 128:75420
TITLE: Preparation of novel derivative of pyrrole-3,4-dicarboxylic acid imide
INVENTOR(S): Malinka, Wiesław; Kleinrok, Zdzisław; Sieklucka, Maria
PATENT ASSIGNEE(S): Akademia Medyczna, Pol.
SOURCE: Pol., 4 pp.
CODEN: POXXA7
DOCUMENT TYPE: Patent
LANGUAGE: Polish
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| PL 172418 | B1 | 19970930 | PL 1993-299531 | 19930701 |

G1



I



II

AB The title compd. I, useful as psychotropic, was prepd. by reacting the imide II with N-(2-chlorophenyl)piperazine in the presence of K₂CO₃ in MeCN. Compd. I reduced the spontaneous activity in mice at 1/80 LD₅₀ (LD₅₀ = 766.3).

IT 159658-13-6P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of novel deriv. of pyrrole-3,4-dicarboxylic acid imide)
RN 159658-13-6 CAPLUS

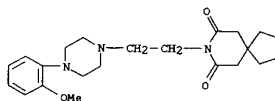
L14 ANSWER 94 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:53477 CAPLUS
 DOCUMENT NUMBER: 128:200886
 TITLE: Discriminative stimulus effects of 8-hydroxy-2-(di-n-propylamino)tetralin in pigeons and rats
 AUTHOR(S): rats: species similarities and differences Kleven, Mark S.; Koek, Wouter
 CORPORATE SOURCE: Centre de Recherche Pierre Fabre, Castres, 81106, Fr.
 SOURCE: Journal of Pharmacology and Experimental Therapeutics
 PUBLISHER: (1998), 284(1), 238-249
 DOCUMENT TYPE: CODEN: JPETAB; ISSN: 0022-3565
 LANGUAGE: Williams & Wilkins
 AB In this study the authors examd. the effects of 5-HT1A ligands in rats trained to discriminate 0.16 mg/kg i.p. 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) from saline in a two-lever, fixed ratio (FR) 10 schedule of food reinforcement, and in pigeons trained to discriminate 0.31 mg/kg i.m. 8-OH-DPAT from saline in a two-key, FR30 schedule of food reinforcement. In both species, 8-OH-DPAT and a variety of structurally unrelated 5-HT1A ligands occasioned dose-related, relatively high levels of drug-appropriate selection (i.e.: .gtoreq.67%). A significant pos. correlation was found between estd. ED50 values in both species (r = 0.84). Further, 5-HT1A antagonists, NAN-190, penbutolol, (-)-pindolol, tertatolol and WAY-100635, produced dose-related decreases in 8-OH-DPAT-appropriate selection, and their potencies for antagonism in rats and pigeons were highly correlated (r = 0.96). The potency of WAY 100635 in rats and pigeons was quantified by Schild anal. (apparent in vivo pA2 values: 7.8 vs. 8.3, rat vs. pigeon, resp.). Although most 5-HT1A agonists produced similar 8-OH-DPAT-like discriminative stimulus effects in both species, two compds., lisuride and eltoprazine, occasioned high levels of drug-appropriate selection in pigeons, but not in rats. In contrast, idazoxan, yohimbine, LEK 8804 and BMY 7378 produced greater effects in rats. Among this latter group of compds., only BMY 7378 blocked the discriminative stimulus effects of 8-OH-DPAT in pigeons, which suggested that intermediate levels of drug-appropriate selection obsd. with the remaining compds. are not necessarily the result of low intrinsic activity. Overall, these results demonstrate similarities in the

L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:9220 CAPLUS
 DOCUMENT NUMBER: 128:110381
 TITLE: Iscindol-1-one Analogs of 4-(2'-methoxyphenyl)-1-[2']-[N-(2''-pyridyl)-p-iodobenzamido]ethyl]piperazine (p-MPPI) as 5-HT1A Receptor Ligands
 AUTHOR(S): Zhuang, Zhi-Ping; Kung, Mei-Ping; Mu, Mu; Kung, Hank
 CORPORATE SOURCE: Departments of Radiology and Pharmacology, University of Pennsylvania, Philadelphia, PA, 19104, USA
 SOURCE: Journal of Medicinal Chemistry (1998), 41(2), 157-166
 PUBLISHER: CODEN: JMCMAJ; ISSN: 0022-2623
 DOCUMENT TYPE: American Chemical Society
 LANGUAGE: English

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

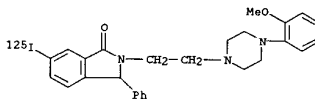
AB In developing radiiodinated antagonists for in vivo imaging of 5-HT1A receptors with SPECT, a series of new arylpiperazine benzamido derivs., including I (p-MPPI) (Kd = 0.36 nM), as potential ligands for 5-HT1A receptors were reported previously. However, rapid in vivo metab. may have caused the breakdown of the amide bond of [123I]-I and rendered this agent obsolete as an in vivo imaging agent in humans. To improve the in vivo stability of I, a series of cyclized amide analogs were designed and synthesized. In vitro binding, metabolic stability, and in vivo biodistribution of these new derivs. were investigated. Several five-membered-ring isocindol-1-ones displayed very high in vitro binding affinity, esp. II (R = H, R1 = NO2; R = OH, R1 = iodo; R = H, R1 = iodo), which showed Ki values of 0.05, 0.65, and 0.07 nM, resp. The affinities for 5-HT1A receptors of other cyclized amide derivs. III (R2 = Br, iodo) and IV, were 1.09, 2.54, and 14.9 nM, resp. Compared to [125I]-I, iodinated cyclized amide derivs. [125I]-II (R = H, R1 = iodo) and [125I]-III (R2 = iodo) displayed a slower metab. in human liver microsomal and cytosolic preps. Biodistribution of [125I]-II (R = H, R1 = iodo) and [125I]-III (R2 = iodo) in rats (after an i.v. injection) displayed moderate to low brain uptakes with little or no specific localization in

L14 ANSWER 94 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 discriminative stimulus effects of 8-OH-DPAT in rats and pigeons despite different training conditions (e.g., training dose and route of administration). Even so, the finding that some 5-HT1A ligands did not produce similar effects in rats and pigeons illustrates the need to examine possible 8-OH-DPAT-like discriminative stimulus effects of compds. in both species.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (discriminative stimulus effects of hydroxy(di-n-propylamino)tetralin in pigeons and rats in relation to species similarities and differences)
 RN 21102-95-4 CAPLUS
 CN 8-Azasp[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

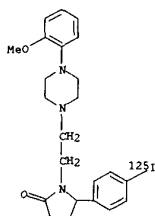


●2 HCl

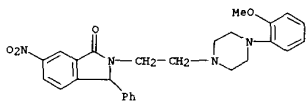
L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 hippocampal region, where 5-HT1A receptors are concd. These data indicate that the new iodinated ligands showed high binding affinities and better metabolic stability but displayed unexpectedly low selective binding to 5-HT1A receptors in vivo. Adnl. structural modifications may be needed to correct the unfavorable properties displayed for these iodinated cyclized amide derivs. for in vivo biodistribution in rats.
 IT 201531-46-6P 201531-47-7P
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic Preparation); BIOL (Biological study); PREP (Preparation); PROC (Process) (prepn. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine isocindolone analogs as serotonin 5-HT1A receptor ligands)
 RN 201531-46-6 CAPLUS
 CN 1H-isocindol-1-one, 2,3-dihydro-6-(iodo-125I)-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



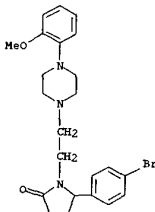
RN 201531-47-7 CAPLUS
 CN 2-Pyrrolidinone, 5-[4-(iodo-125I)phenyl]-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



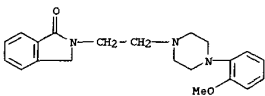
IT 201531-35-3P 201531-36-4P 201531-37-5P
 201531-40-0P 201531-42-2P
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation);
 BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine
 isoindolone analogs as serotonin 5-HT_{1A} receptor ligands)
 RN 201531-35-3 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-{4-(2-methoxyphenyl)-1-
 piperazinyl}ethyl]-6-nitro-3-phenyl- (9CI) (CA INDEX NAME)



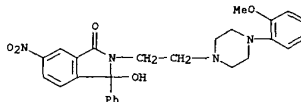
RN 201531-36-4 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-{4-(2-methoxyphenyl)-1-
 piperazinyl}ethyl]-6-nitro-3-phenyl- (9CI) (CA INDEX NAME)



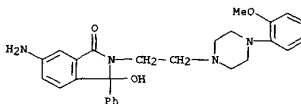
IT 99718-69-1P 201531-33-1P 201531-34-2P
 201531-38-6P 201531-39-7P 201531-41-1P
 201531-44-4P
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological
 study); PREP (Preparation)
 (prepn. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine
 isoindolone analogs as serotonin 5-HT_{1A} receptor ligands)
 RN 99718-69-1 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-{4-(2-methoxyphenyl)-1-
 piperazinyl}ethyl]- (9CI) (CA INDEX NAME)



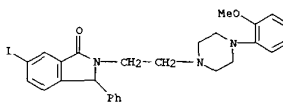
RN 201531-33-1 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-{4-(2-methoxyphenyl)-1-
 piperazinyl}ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



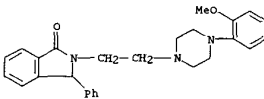
RN 201531-37-5 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-{4-(2-methoxyphenyl)-
 1-piperazinyl}ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



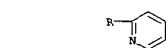
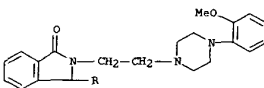
RN 201531-40-0 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-6-iodo-2-[2-{4-(2-methoxyphenyl)-1-
 piperazinyl}ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



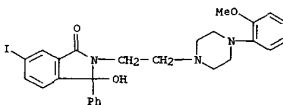
RN 201531-42-2 CAPLUS
 CN 2-Pyrrolidinone, 5-(4-bromophenyl)-1-[2-{4-(2-methoxyphenyl)-1-
 piperazinyl}ethyl]- (9CI) (CA INDEX NAME)



RN 201531-34-2 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-2-[2-{4-(2-methoxyphenyl)-1-
 piperazinyl}ethyl]-3-(2-pyridinyl)- (9CI) (CA INDEX NAME)

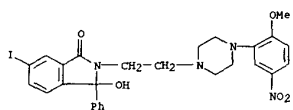


RN 201531-38-6 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-6-iodo-2-[2-{4-(2-methoxyphenyl)-
 1-piperazinyl}ethyl]-3-phenyl- (9CI) (CA INDEX NAME)

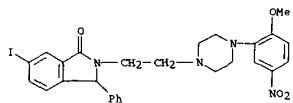


RN 201531-39-7 CAPLUS
 CN 1H-Isoindol-1-one, 2,3-dihydro-3-hydroxy-6-iodo-2-[2-{4-(2-methoxy-5-
 nitrophenyl)-1-piperazinyl}ethyl]-3-phenyl- (9CI) (CA INDEX NAME)

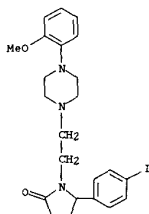
L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 201531-41-1 CAPLUS
CN 1H-isindol-1-one, 2,3-dihydro-6-iodo-2-[2-(4-(2-methoxy-5-nitrophenyl)-1-piperazinyl)ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



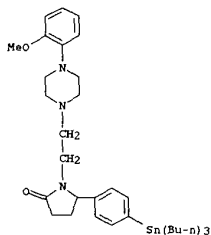
RN 201531-44-4 CAPLUS
CN 2-Pyrrolidinone, 5-(4-iodophenyl)-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



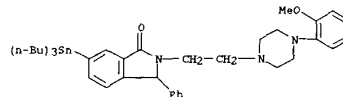
IT 201531-43-3P 201531-45-5P 201532-02-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT (Reactant or reagent)
(prepn. of (methoxyphenyl)[(pyridyl)iodobenzamidoethyl]piperazine

L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

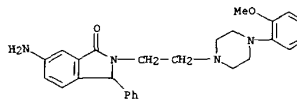
L14 ANSWER 95 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
isindolone analogs as serotonin 5-HT1a receptor ligands
RN 201531-43-3 CAPLUS
CN 2-Pyrrolidinone, 1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-5-[4-(tributylstannyl)phenyl]- (9CI) (CA INDEX NAME)



RN 201531-45-5 CAPLUS
CN 1H-isindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl-6-(tributylstannyl)- (9CI) (CA INDEX NAME)

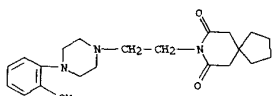


RN 201532-02-7 CAPLUS
CN 1H-isindol-1-one, 6-amino-2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3-phenyl- (9CI) (CA INDEX NAME)



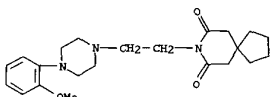
L14 ANSWER 96 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:6089 CAPLUS
DOCUMENT NUMBER: 128:149828
TITLE: Pharmacological evidence for
.alpha.1D-adrenoceptors
in the rabbit ventricular myocardium: analysis
with
BMV 7378
AUTHOR(S): Yang, Tuang-Tian; Endoh, Masao
CORPORATE SOURCE: Department of Pharmacology, Yamagata University
School
of Medicine, Yamagata, 990-23, Japan
SOURCE: British Journal of Pharmacology (1997), 122(8),
1541-1550
CODEN: BJPCMH; ISSN: 0007-1188
PUBLISHER: Stockton Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It was examd. by means of BMV 7378, a selective antagonist of
.alpha.1D-adrenoceptors, whether .alpha.1D-adrenoceptors contribute
to the
regulation of myocardial contractility and hydrolysis of
phosphoinositide
(PI) in rabbit ventricular muscle. BMV 7378 had a biphasic
antagonistic
action on the pos. inotropic effect (PIE) of phenylephrine depending
on
the concn. BMV 7378 at 1-10 nM shifted the concn.-response curve
(CRC)
for the PIE of phenylephrine to the right and downward and at 100 nM
to 1
.mu.M it antagonized the PIE in a competitive manner, the slope of
Schild
plot being 0.93 and the pA2 being 7.17+/-0.09. The inhibitory
action of
BMV 7378 at 1-10 nM is ascribed to the selective action on
.alpha.1-adrenoceptors because the PIE of neither isoprenaline nor
endothelin-3 and angiotensin II was affected by this compd. over this
concn. range. In the presence of 100 nM WB 4101, the antagonistic
action
of BMV 7378 at 1-10 nM remained unchanged but the antagonistic action
of
BMV 7378 at 100-300 nM disappeared. The antagonistic action of BMV
7378
at 1 nM was unaffected by 100 nM (+)-niguldipine. Following
pretreatment
with chloroethylclonidine, BMV 7378 at 1 nM inhibited the maximal
response
to phenylephrine but the pD2 value for phenylephrine was increased in
the
presence of BMV 7378. The CRC for phenylephrine was shifted to the
left
in the presence of 10-100 nM BMV 7378 but it was shifted to the right
by
BMV 7378 at 300 nM. Stimulation of PI hydrolysis induced by
phenylephrine
was not affected by BMV 7378 up to 10 nM but it was reduced
significantly

L14 ANSWER 96 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 by BMY 7378 at higher concns. (100 nM to 1 .mu.M). BMY 7378
 inhibited the
 [3H]prazosin specific binding to the rabbit ventricular membrane
 fraction
 in a monophasic manner with a pKi value of 7.53+/-0.09. The results
 indicate that in rabbit ventricular muscle, BMY 7378 at 1-10 nM
 suppressed
 the maximal response to phenylephrine (probably mediated by
 .alpha.1D-adrenoceptors) and at 10-100 nM it inhibited the neg.
 inotropic
 effect of phenylephrine, the mechanisms of which remain to be
 characterized. At higher concns. (100 nM to 1 .mu.M) BMY 7378
 antagonized
 the functional and biochem. response via a presumed interaction
 mainly
 with the .alpha.1B-adrenoceptor and partially with the
 .alpha.1A-adrenoceptor.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); BIOL (Biological study)
 (Pharmacol. evidence for .alpha.1D-adrenoceptors in rabbit
 ventricular
 myocardium using BMY 7378)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 97 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 indicate that the alpha-1B AR mediates the contraction of only the
 mesenteric resistance artery.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); BUU (Biological use, unclassified); BIOL
 (Biological
 study); USES (Uses)
 (.alpha.-adrenergic receptor subtype localization and
 contribution to
 vascular smooth muscle contraction)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

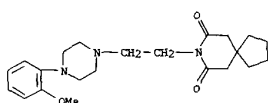


●2 HCl

L14 ANSWER 97 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:749539 CAPLUS
 DOCUMENT NUMBER: 128:44122
 TITLE: Immunocytochemical localization of the alpha-1B
 adrenergic receptor and the contribution of this
 and
 the other subtypes to vascular smooth muscle
 contraction: analysis with selective ligands and
 antisense oligonucleotides
 AUTHOR(S): Piascik, Michael T.; Hrometz, Sandra L.; Edelmann,
 Stephanie E.; Guarino, Richard D.; Hadley, Robert
 W.;
 CORPORATE SOURCE: Brown, R. Dale
 Department of Pharmacology and Vascular Biology
 Research Group, University of Kentucky College of
 Medicine, Lexington, KY, USA
 SOURCE: Journal of Pharmacology and Experimental
 Therapeutics
 (1997), 283(2), 854-868
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: Williams & Wilkins
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The contribution of the alpha-1B adrenergic receptor (AR) to vascular
 smooth muscle contraction has been assessed using a combination of
 immunol., mol. biol. and pharmacol. approaches. A subtype-selective
 antibody detected alpha-1B immunoreactivity in the medial layer of the
 aorta, caudal, femoral, iliac, mesenteric resistance, renal and
 superior
 mesenteric arteries. Receptor protection assays and antisense
 oligonucleotides were used to assess the contribution of the alpha-1B
 AR
 to contraction. The alpha-1B AR was implicated in mediating the
 phenylephrine-induced contraction of the mesenteric resistance artery.
 The alpha-1D AR was implicated in mediating the contraction of the
 aorta,
 femoral, iliac and superior mesenteric arteries. Similarly, the
 alpha-1A
 AR was implicated in mediating contraction of the caudal and renal
 arteries. In vivo application of antisense oligonucleotides targeted
 to
 the translational start site of the alpha-1B AR had no effect on the
 phenylephrine-induced contraction of the femoral or renal arteries.
 In
 contrast, antisense oligonucleotides directed against the alpha-1D AR
 significantly inhibited the phenylephrine response in the femoral
 artery
 but had no effect on the renal artery. Application of alpha-1A AR
 antisense oligonucleotides inhibited the contraction of the renal
 artery
 without effect on the femoral artery. These data show that (1)
 alpha-1B
 AR immunoreactivity is widely distributed in the same peripheral
 arteries
 in which previous studies detected its mRNA, and (2) despite this
 distribution, receptor protection and antisense oligonucleotide
 studies

L14 ANSWER 98 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:720998 CAPLUS
 DOCUMENT NUMBER: 128:18934
 TITLE: Investigation of .alpha.1-adrenoceptor subtypes
 mediating vasoconstriction in rabbit cutaneous
 resistance arteries
 AUTHOR(S): Smith, K. M.; Macmillan, J. B.; McGrath, J. C.
 CORPORATE SOURCE: Clinical Research Initiative in Heart Failure,
 Neuroscience and Biomedical Systems, University of
 Glasgow, Glasgow, G12 8QQ, UK
 SOURCE: British Journal of Pharmacology (1997), 122(5),
 825-832
 CODEN: BJPCBM; ISSN: 0007-1188
 PUBLISHER: Stockton
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Cutaneous resistance arteries (c.r.a.) (internal diam.=240.94+/-5.42
 .mu.m, n=67/25 (no. arteries/no. animals)) from New Zealand white
 rabbits
 were mounted in wire myographs and a normalization procedure followed.
 Cumulative concn.-response curves (CPRCs) were constructed for the
 .alpha.-adrenoceptor agonists noradrenaline (NA), (R)A61603 and
 phenylephrine (PE) in the presence of cocaine (3 .mu.M), propranolol
 (1
 .mu.M) and corticosterone (10 .mu.M). The effects of competitive
 .alpha.1-adrenoceptor antagonists, prazosin, WB4101,
 5-methyl-urapidil,
 HV723, BMY7378 and the irreversible .alpha.1B selective compd.
 chloroethylclonidine (CEC) were examd. vs. the potency and max.
 response
 of the c.r.a.s to noradrenaline. The high potency of A-61603
 relative to
 PE has been shown to differentiate both functional and binding site
 .alpha.1A- or .alpha.1B-adrenoceptors from .alpha.1D-adrenoceptors:
 A-61603 was 944 times more potent than phenylephrine (at EC50)
 suggesting
 the presence of a functional .alpha.1A or .alpha.1B as opposed to an
 .alpha.1D-subtype. Exposure to chloroethylclonidine (CEC) 100 .mu.M
 decreased the max. response to noradrenaline but did not significantly
 change noradrenaline sensitivity indicating that a substantial part of
 noradrenaline-induced vasoconstriction in rabbit cutaneous arteries is
 CEC-insensitive. The potencies of prazosin (pA2 = 9.14) and WB4101
 (pA2 =
 9.30) indicate the involvement of prazosin-sensitive functional
 .alpha.1-adrenoceptors. The slopes of corresponding Schild plots for
 prazosin and WB4101 did not include neg. unity which implies the
 possible
 involvement of more than one functional .alpha.1-adrenoceptor subtype
 in
 noradrenaline-induced vasoconstriction in rabbit cutaneous resistance
 arteries. In contrast to this, in the case of 5-methyl-urapidil and
 HV723, the Schild plot slope parameters were not significantly
 different
 from neg. unity over the range of concns. used; the low pA2 value for
 5-methylurapidil (7.27) suggests the non-involvement of an .alpha.1A-
 or
 an .alpha.1D-adrenoceptor; the low pA2 value for HV723 (8.47) was
 similar

L14 ANSWER 98 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 to that against responses postulated as .alpha.1L. The authors
 conclude
 that rabbit cutaneous resistance arteries express a
 prazosin-sensitive
 functional .alpha.1-adrenoceptor resembling the .alpha.1B and
 another low
 affinity site for prazosin which on the basis of the functional
 antagonism
 produced by HV723 most closely resembles the .alpha.1L-adrenoceptor;
 the
 low pA2 value for HV723 (8.47) is similar to that against responses
 postulated as .alpha.1L.
 IT 21102-95-4, BM7378
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
 (Uses)
 (.alpha.1-adrenoceptor subtypes mediating vasoconstriction in
 rabbit
 cutaneous resistance arteries)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-{2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl}-, dihydrochloride (9CI) (CA INDEX NAME)

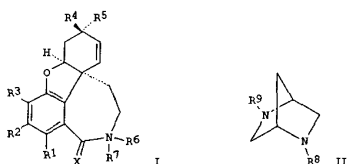


● 2 HCl

L14 ANSWER 99 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:717921 CAPLUS
 DOCUMENT NUMBER: 128:13368
 TITLE: New benzazepine derivatives, medicaments
 containing
 the same and their use to prepare medicaments
 INVENTOR(S): Czollner, Laszlo; Frohlich, Johannes; Jordis,
 Ulrich;
 Kuenburg, Bernhard
 PATENT ASSIGNEE(S): Sanocemia Ltd., Malta; Czollner, Laszlo;
 Frohlich,
 Johannes; Jordis, Ulrich; Kuenburg, Bernhard
 SOURCE: PCT Int. Appl., 136 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

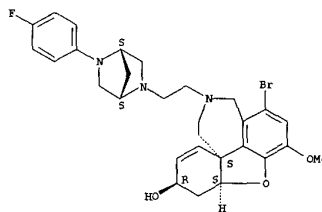
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9740049 | A1 | 19971030 | WO 1997-AT74 | 19970421 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, | | | | |
| DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, | | | | |
| LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, | | | | |
| PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, | | | | |
| VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, | | | | |
| GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, | | | | |
| GN, ML, MR, NE, SN, TD, TG | | | | |
| AT 9600716 | A | 19971015 | AT 1996-716 | 19960419 |
| AT 403803 | B | 19980525 | | |
| AU 9724985 | A1 | 19971112 | AU 1997-24985 | 19970421 |
| EP 897387 | A1 | 19990224 | EP 1997-516263 | 19970421 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, FI | | | | |
| NO 9804852 | A | 19981116 | NO 1998-4852 | 19981016 |
| PRIORITY APPLN. INFO.: | | | AT 1996-716 | 19960419 |
| | | | WO 1997-AT74 | 19970421 |
| OTHER SOURCE(S): MARPAT 128:13368 | | | | |
| GI | | | | |

L14 ANSWER 99 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



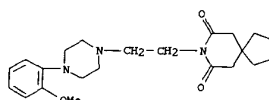
AB The synthesis of benzofuro[3a,3,2,ef][2]benzazepines (I) [R1,R2 = H,
 halo,
 CN, NC, OH, SH, SO3H, NH2, CF3, (un)substituted alkyl,
 (un)substituted
 alkoxy, (un)substituted aryl, (un)substituted aryloxy; R3 = OH, OMe;
 R4,R5
 = H2, O, substituted O, (un)substituted alkyl, (un)substituted aryl,
 (un)substituted alkenyl, (un)substituted alkynyl, (un)substituted
 hydrazone, (un)substituted oxime; X = H2, O] and
 diazabicyclo[2.2.1]heptanes (II) [R8 = CH2Ph, 4-MeC6H4SO2, H,
 (un)substituted alkyl, Me3CO2C; R9 = (un)substituted Ph, CH2Ph,
 CHPh2,
 Me3CO2C] are described. Thus, I (R1 = Br, R2 = H, R3 = OMe, R4 =
 OH, R5 =
 H, R6 = H, X = H2) (III) was prepd. by tartrate resolin. of
 (+..)-N-demethyl-8-bromogalanthamine. III in in vitro study showed
 an
 IC50 of >150 in .upsilon.mol for the inhibition of acetylcholine
 esterase.
 Also disclosed are medicaments which contain compds. of formulas (I)
 and/or (II) and may be successfully used for treating Alzheimer
 disease
 and related demential states, as well as the Langdon-Down syndrome.
 IT 198988-64-6P
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
 use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of benzazepine galanthamine analogs and
 diazabicycloheptanes
 for use in treatment of dementia)
 RN 198988-64-6 CAPLUS
 CN 6H-Benzofuro[3a,3,2,ef][2]benzazepin-6-ol, 1-bromo-11-[2-[5-(4-
 fluorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]ethyl]-4a,5,9,10,11,12-
 hexahydro-3-methoxy-, (4a.alpha.,6.beta.,8aR*,11(1R*,4R*))]- (9CI)
 (CA
 INDEX NAME)

L14 ANSWER 99 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 Relative stereochemistry.



L14 ANSWER 100 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:713805 CAPLUS
 DOCUMENT NUMBER: 128:18928
 TITLE: Antagonism to noradrenaline-induced lethality in rats
 is related to affinity for the .alpha.1A-adrenoceptor subtype
 AUTHOR(S): Testa, Rodolfo; Guarneri, Luciano; Ibba, Marina; Angelico, Patrizia; Poggesi, Elena; Taddei, Carlo;
 CORPORATE SOURCE: Motta, Gianni; Leonardi, Amedeo
 Pharmaceutical RandD Division, RECORDATI S.p.A., Milan, 20148, Italy
 SOURCE: Life Sciences (1997), 61(22), 2177-2188
 CODEN: LIFSAK; ISSN: 0024-3205
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The potency of several .alpha.1-adrenoceptor antagonists in preventing the noradrenaline-induced lethality in conscious rats, their binding affinity for the native .alpha.1A- and .alpha.1B-adrenoceptors, the recombinant animal .alpha.1A-, .alpha.1B- and .alpha.1D-adrenoceptor subtypes, as well as their functional affinity for the .alpha.1L-adrenoceptor subtype were evaluated. The potency of the tested compds. as antagonists of noradrenaline-induced lethality was correlated with the affinity for the .alpha.1A- (and .alpha.1A-) adrenoceptor subtype, but not with the affinity for the other subtypes. On the contrary, the hypotensive effects of the compds., assessed in anesthetized rats, were not clearly related with the affinity for any of the .alpha.1-subtypes. These results suggest that the .alpha.1A-subtype plays a detg. role in preventing lethality induced by noradrenaline in the rats, and that this activity is unrelated to the hypotensive effect of the compds., which cannot be clearly correlated with affinity for a particular .alpha.1-adrenoceptor subtype.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 [antagonism to noradrenaline-induced lethality relation to affinity for .alpha.1A-adrenoceptor subtype]
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 100 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

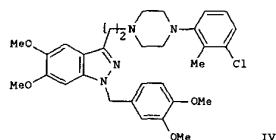
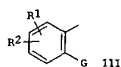
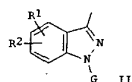


●2 HCl

L14 ANSWER 101 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:701490 CAPLUS
 DOCUMENT NUMBER: 128:22921
 TITLE: Preparation of piperazines having calmodulin inhibitory activity
 INVENTOR(S): Yamamoto, Kenjiro; Hasegawa, Atsushi; Kubota, Hideki;
 PATENT ASSIGNEE(S): AndoDeceased, Masahiro; Yamaguchi, Hitoshi
 SOURCE: Daiichi Pharmaceutical Co., Ltd., Japan U.S., 44 pp., Cont.-in-part of U.S. Ser. No. 242,842,
 abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

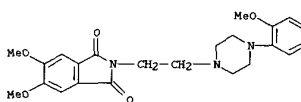
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| US 5681954 | A | 19971028 | US 1995-416311 | 19950404 |
| PRIORITY APPLN. INFO.: | | | JP 1993-11277 | 19930514 |
| | | | US 1994-242842 | 19940516 |

 OTHER SOURCE(S): MARPAT 128:22921
 GI

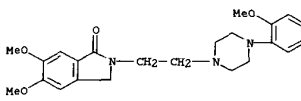


AB The title compds. [I; Q = Cl-6 alkyl, Cl-6 alkoxy, CF3, etc.; R = I or
 or III (wherein G = Cl-6 alkyl, (un)substituted Ph, etc.; R1, R2 = Cl-6 alkyl, Cl-6 alkoxy, CF3, etc.); Z = Cl-3 alkylene, C2-4 alkenylene, C(=O), etc.], useful as a treating agent for diseases in the circulatory organs

L14 ANSWER 101 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 or in the cerebral region which are caused by excessive activation of calmodulin, were prepd. Thus, treatment of 1-([5,6-dimethoxy-1-(3,4-dimethoxybenzyl)-1H-indazol-3-yl]acetyl)-4-(3-chloro-2-methylphenyl)piperazine with BH3*THF in THF afforded the title compd.
 IV which showed 19.24 increase of survival time on nitrogen-induced hypoxia model in mouse, and IC50 of 3.1 against calmodulin-dependent PDE.
 IT 198980-97-1P 198981-00-9P 198981-05-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of piperazines having calmodulin inhibitory activity)
 RN 198980-97-1 CAPLUS
 CN 1H-Isolindole-1,3(2H)-dione, 5,6-dimethoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



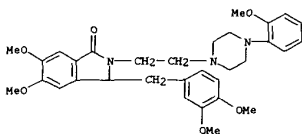
RN 198981-00-9 CAPLUS
 CN 1H-Isolindole-1-one, 3-[1-(3,4-dimethoxyphenyl)methyl]-2,3-dihydro-5,6-dimethoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 198981-05-4 CAPLUS
 CN 1H-Isolindole-1-one, 3-[1-(3,4-dimethoxyphenyl)methyl]-2,3-dihydro-5,6-dimethoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 101 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



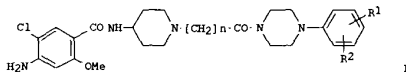
●2 HCl

L14 ANSWER 102 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:618726 CAPLUS
DOCUMENT NUMBER: 127:293254
TITLE: Preparation of
N-(1-substituted-4-piperidyl)benzamide
having serotonin receptor agonist activity
INVENTOR(S): Vladimir
Aleksievich Shimamura, Masahiro Ikeda, Akira
Kobayashi, Hideyuki Chaki, Etsuko Takahashi,
Kazuyoshi
PATENT ASSIGNEE(S): Morishita Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JXXXXF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 09241241 | A2 | 19970916 | JP 1996-80693 | 19960308 |

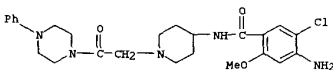
OTHER SOURCE(S): HARPAT 127:293254
G1



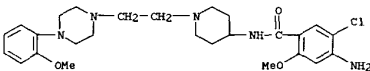
AB Title compds. I (R1, R2 = H, halo, lower alkoxy, lower alkyl; X = CO, methylene; n = 1-3) and their pharmaceutically acceptable salts are prepd.
4-Amino-5-chloro-2-methoxy-N-(4-piperidyl)benzamide hydrochloride was treated with
1-(3-chloro-1-oxo-1-propyl)-4-(2-methoxyphenyl)piperazine in HCONMe2 in the presence of Na2CO3 and NaI at 80.degree. for 4 h to give
97% I (R1 = 2-MeO, R2 = H, X = CO, n = 2) (II), which was treated with oxalic acid in MeOH to give 1.61 g II oxalate. II oxalate showed EC50 of 20.5 nM for relaxation of carbachol-contracted esophageal smooth muscle of a rat.
IT 197069-60-6P 197069-63-9P 197069-68-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(prepn. of N-(1-substituted-4-piperidyl)benzamide having serotonin agonist activity)

L14 ANSWER 102 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

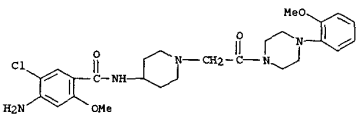
RN 197069-60-6 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 197069-63-9 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



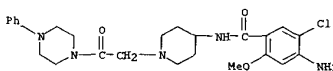
RN 197069-68-4 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]-4-piperidinyl]- (9CI) (CA INDEX NAME)



IT 197069-61-7P 197069-64-0P 197069-69-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of N-(1-substituted-4-piperidyl)benzamide having serotonin agonist activity)
RN 197069-61-7 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-4-piperidinyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

L14 ANSWER 102 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CH 1
CRN 197069-60-6
CHF C25 H32 Cl N5 O3

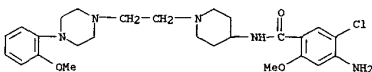


CH 2
CRN 144-62-7
CHF C2 H2 O4



RN 197069-64-0 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4-piperidinyl]-, ethanedioate (1:1) (9CI) (CA INDEX NAME)

CH 1
CRN 197069-63-9
CHF C26 H36 Cl N5 O3

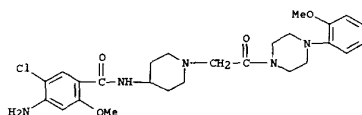


CH 2
CRN 144-62-7
CHF C2 H2 O4



L14 ANSWER 102 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 197069-69-5 CAPLUS
CN Benzamide, 4-amino-5-chloro-2-methoxy-N-[1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-2-oxoethyl]-4-piperidinyl]-, ethanedioate (1:1) (9CI)
(CA INDEX NAME)
CM 1
CFN 197069-68-4
CMF C26 H34 Cl N5 O4



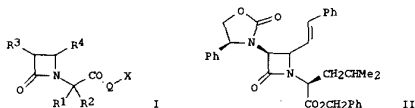
CM 2
CFN 144-62-7
CMF C2 H2 O4



L14 ANSWER 103 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:576686 CAPLUS
DOCUMENT NUMBER: 127:234215
TITLE: Preparation of non-peptidyl vasopressin Vla receptor antagonists
INVENTOR(S): Bruns, Robert F., Jr.; Cooper, Robin D. G.; Dressman, Bruce A.; Hunden, David C.; Kaldor, Stephen W.; Koppel, Gary A.; Rizzo, John R.; Skelton, Jeffrey James; et al.
PATENT ASSIGNEE(S): Eli Lilly and Co., USA; Bruns, Robert F., Jr.; Cooper, Robin D. G.; Dressman, Bruce A.; Hunden, David C.; Kaldor, Stephen W.; Koppel, Gary A.
SOURCE: PCT Int. Appl., 158 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

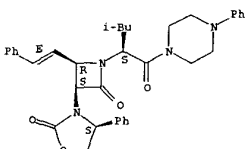
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|-------------------|-----------------|-------------|
| WO 9730707 | A1 | 19970828 | WO 1997-US3039 | 19970220 |
| W: | AL, AM, AT, AU, A2, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, HW: KE, LS, MW, SD, SE, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, MR, NE, SN, TD, TG | | | |
| AU 9719779 | A1 | 19970910 | AU 1997-19779 | 19970220 |
| EP 939632 | A1 | 19990908 | EP 1997-907895 | 19970220 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI | | | |
| JP 2000504731 | T2 | 20000418 | JP 1997-529647 | 19970220 |
| US 6204260 | B1 | 20010320 | US 1999-125737 | 19990819 |
| US 2002049187 | A1 | 20020425 | US 2000-733430 | 20001208 |
| PRIORITY APPLN. INFO.: | | | US 1996-12149P | P 19960223 |
| | | | US 1996-12188P | P 19960223 |
| | | | US 1996-12215P | P 19960223 |
| | | | GB 1996-5044 | A 19960309 |
| | | | GB 1996-5045 | A 19960309 |
| | | | GB 1996-5046 | A 19960309 |
| | | | WO 1997-US3039 | W 19970220 |
| | | | US 1999-125737 | A3 19990819 |
| OTHER SOURCE(S): | | MARPAT 127:234215 | | |
| GI | | | | |

L14 ANSWER 103 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB Azetidinones I [R1 = H, alkyl, carbamoyl, alkoxy, acyl, benzoyl, phenyl; R2 = H, OH, alkyl; R3 = phthalimido, azido, phenoxycetamido, oxazoliny, imidazoliny, pyrrolidinyl, ureido; Q = O, S, NR5; X = H, alkyl; R5 = H, alkyl, OH, alkoxy, carbonyl, benzyl] were prep. for use as vasopressin Vla receptor antagonists. Thus, azetidinone II was prep. starting from L-leucine benzyl ester, cinnamaldehyde, and 2-[4(5)-phenyloxazolidin-2-on-3-yl]acetyl chloride. II gave an IC50 value of 39 nM when tested for vasopressin Vla receptor binding affinity.
IT 195310-53-3P
RU: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of non-peptidyl vasopressin Vla receptor antagonists)
RN 195310-53-3 CAPLUS
CN Piperazine, 1-[4-methyl-1-oxo-2-[2-oxo-3-(2-oxo-4-phenyl-3-oxazolidinyl)-4-(2-phenylethenyl)-1-azetidinyl]pentyl]-4-phenyl-, [3S-[1(R*),3.alpha.(R*),4.alpha.(E)]]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

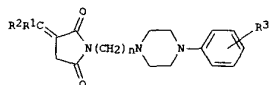


L14 ANSWER 103 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:549258 CAPLUS
 DOCUMENT NUMBER: 127:149085
 TITLE: arylpiperazinylalkylsuccinimides with 5-HT1A and adrenergic.alpha.1 affinity
 INVENTOR(S): Lopez Rodriguez, Ma. Luz; Morcillo Ortega, Ma. Jose;
 Rosado K. Rovat, Tandu; Fernandez Velando, Esther;
 Samitier, Ma. Luisa; Oresanz Muno, Luis Miguel
 PATENT ASSIGNEE(S): Universidad Complutense De Madrid, Spain
 SOURCE: Span., 10 pp.
 CODEN: SPXXAD
 DOCUMENT TYPE: Patent
 LANGUAGE: Spanish
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

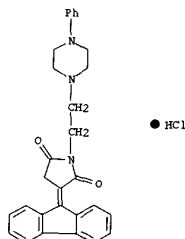
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| ES 2094690 | A1 | 19970116 | ES 1994-2396 | 19941122 |
| ES 2094690 | B1 | 19970801 | | |

OTHER SOURCE(S): MARPAT 127:149085
 GI

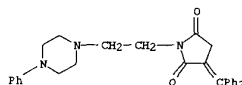


AB Title compds. I [R1, R2 = Ph, R1R2 = o-C6H4C6H4-o; R3 = H, alkyl, halogen, alkoxy; n = 1-4] were prepd. Thus, fluorenone was treated with succinonitrile to give 3-(9H-fluoren-9-ylidene)pyrrolidine-2,5-dione which was treated with 1-(3-trifluoromethylphenyl)piperazine to give I [R1R2 = o-C6H4C6H4-o, R3 = 3-CF3, n = 1, II]. II had 5-HT1A affinity of 44.1 nM and .alpha.1 affinity of >1000 nM.
 IT 193287-12-6P 193287-13-7P 193287-14-8P
 193287-15-9P 193287-16-0P 193287-17-1P
 193287-18-2P 193287-19-3P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepa. of arylpiperazinylalkylsuccinimides with 5-HT1A and adrenergic.alpha.1 affinity)
 RN 193287-12-6 CAPLUS

L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

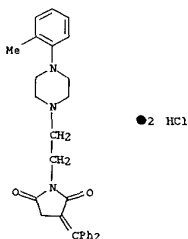


RN 193287-13-7 CAPLUS
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

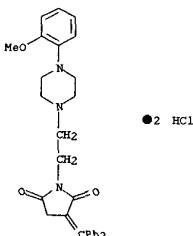


RN 193287-14-8 CAPLUS
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

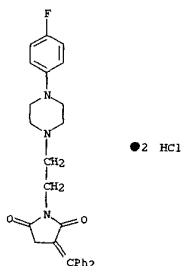


RN 193287-15-9 CAPLUS
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

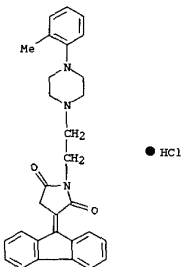


RN 193287-16-0 CAPLUS
 CN 2,5-Pyrrolidinedione, 3-(diphenylmethylene)-1-[2-(4-(4-fluorophenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

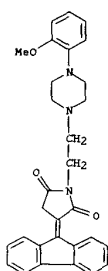
L14 ANSWER 104 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 193287-17-1 CAPLUS
 CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-(4-(2-methylphenyl)-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



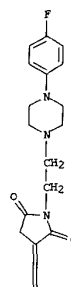
RN 193287-18-2 CAPLUS
 CN 2,5-Pyrrolidinedione, 3-(9H-fluoren-9-ylidene)-1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

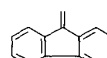
RN 193287-19-3 CAPLUS
CN 2,5-Pyrrolidinedione,
3-[2-(4-(4-methoxyphenyl)-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

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● HCl

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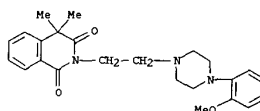


L14 ANSWER 105 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:532196 CAPLUS
DOCUMENT NUMBER: 127:200050
TITLE: Nitrosated and nitrosylated .alpha.-adrenergic receptor antagonist compounds, preparation thereof,
treatment of human impotence or erectile dysfunction
INVENTOR(S): Garvey, David S.; Schroeder, Joseph D.; Saez De Tejada, Inigo
PATENT ASSIGNEE(S): NitroMed, Inc., USA; Garvey, David S.; Schroeder, Joseph D.; Saez De Tejada, Inigo
SOURCE: PCT Int. Appl., 96 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9727749 | A1 | 19970807 | WO 1997-US1294 | 19970128 |
| W: AU, CA, IL, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| AU 9717562 | A1 | 19970822 | AU 1997-17562 | 19970128 |
| AU 721247 | B2 | 20000629 | | |
| JP 2000050424 | T2 | 20000509 | JP 1997-537755 | 19970128 |
| EP 1018879 | A1 | 20000719 | EP 1997-904887 | 19970128 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| US 6294517 | B1 | 20010925 | US 1998-145143 | 19980901 |
| US 6323211 | B1 | 20011127 | US 1999-285048 | 19990402 |
| US 6417162 | B1 | 20020709 | US 1999-306809 | 19990507 |
| US 6433182 | B1 | 20020813 | US 1999-306805 | 19990507 |
| PRIORITY APPLM. INFO.: US 1996-595732 A 19960202 | | | | |
| US 1996-714313 A 19960918 | | | | |
| WO 1997-US1294 W 19970128 | | | | |
| US 1998-145143 A2 19980901 | | | | |

OTHER SOURCE(S): MARPAT 127:200050
AB Disclosed are nitrosated and nitrosylated .alpha.-adrenergic receptor antagonists; compns. of an .alpha.-adrenergic receptor antagonist optionally substituted with .gtoreq.1 NO or NO2 moiety, and a compd. that donates, transfers, or releases nitric oxide as a charged species, i.e., nitrosonium or nitroxyl, or as the neutral species, nitric oxide; and uses for each of them in treating human impotence or erectile dysfunction. Prepn. of compds. of the invention, e.g. N-(N-L-gamma-glutamyl-S-nitroso-L-cysteinyglycine and 4-[2-(dimethylamino)ethoxy]-2-methyl-5-(1-methylethyl)phenol-(3-S-nitroso-3-methylbutyric acid)ester. The effect of selected compds. on erectile response in rabbits was detd.

L14 ANSWER 105 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
IT 67339-62-2, ARC 239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study);
USES (Uses)
(nitrosated and nitrosylated .alpha.-adrenergic receptor antagonist compds., prepn., compns., adrenergic antagonist-NO donor combinations, and use in treatment of human impotence or erectile dysfunction)
RN 67339-62-2 CAPLUS
CN 1,3-(2H,4H)-Isoquinolinedione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



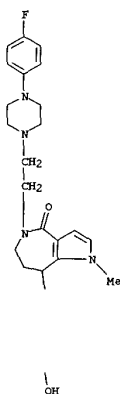
L14 ANSWER 106 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:461620 CAPLUS
DOCUMENT NUMBER: 127:81465
TITLE: Preparation of pyrrolazepine derivatives as
serotonin-2 receptor antagonists
INVENTOR(S): Mizuno, Akira; Shibata, Makoto; Iwamori, Tomoe;
Shimamoto, Tetsuo; Nakanishi, Kyoko; Inomata, Norio
PATENT ASSIGNER(S): Suntory Limited, Japan; Mizuno, Akira; Shibata,
Makoto; Iwamori, Tomoe; Shimamoto, Tetsuo;
Nakanishi, Kyoko; Inomata, Norio
SOURCE: PCT Int. Appl., 160 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------------|---------------|-----------------|----------------------------|
| WO 9720845 | A1 | 19970612 | WO 1996-JP3522 | 19961202 |
| W: AU, CA, HU, IL, JP, KR, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, | | | | |
| PT, SE | CA 2212092 | AA 19970612 | CA 1996-2212092 | 19961202 |
| | AU 9676558 | A1 19970627 | AU 1996-76558 | 19961202 |
| | AU 719230 | B2 20000504 | | |
| | EP 807632 | A1 19971119 | EP 1996-939340 | 19961202 |
| | EP 807632 | B1 20020417 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, | | | | |
| PT, | IE, FI | IL 121432 | A1 20000928 | IL 1996-121432 |
| | | AT 216388 | E 20020515 | AT 1996-939340 |
| | | US 5962448 | A 19991005 | US 1997-875495 |
| | | US 6258805 | B1 20010710 | US 1999-312713 |
| | | US 2002072515 | A1 20020613 | US 2001-801816 |
| PRIORITY APPLN. INFO.: JP 1995-335714 A 19951201 | | | | |
| | | | | JP 1996-46928 A 19960209 |
| | | | | WO 1996-JP3522 W 19961202 |
| | | | | US 1997-875495 A2 19970821 |
| | | | | US 1999-312713 A1 19990517 |
| OTHER SOURCE(S): MARPAT 127:81465 | | | | |
| GI | | | | |

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. (I; ring P = (un)substituted pyrrole ring; A =
alkylene,
alkenylene, alkynylene; Y = N-contg. heterocyclyl, etc; Z1, E2 = H,
lower
alkyl; dotted line = bond or none) are prepd. I, having a potent
serotonin-2 receptor antagonism, are reduced in toxicity and side
effects,

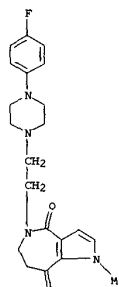
L14 ANSWER 106 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN Pyrrolo[3,2-c]azepin-4(1H)-one, 5-[2-[4-(4-fluorophenyl)-1-
piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-hydroxy-1-methyl- (9CI) (CA
INDEX NAME)



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L14 ANSWER 106 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
and are useful as therapeutic agents for circulatory diseases such as
ischemic heart diseases, cerebrovascular disorders, and peripheral
circulatory disturbances. Thus, pyrrolazepine deriv. (II) (prepn.
given)
was reacted with HSCH₂CH₂SH in the presence of BF₃.Et₂O in AcOH to
give
79% the title compd. (III), which at 10⁻⁸ M showed 75.5% inhibitory
activity against serotonin (5-HT).
IT 191591-85-2P 191592-08-2P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of pyrrolazepine derivs. as serotonin-2 receptor
antagonists)
RN 191591-85-2 CAPLUS
CN Pyrrolo[3,2-c]azepine-4,8(1H,5H)-dione, 5-[2-[4-(4-fluorophenyl)-1-
piperazinyl]ethyl]-6,7-dihydro-1-methyl- (9CI) (CA INDEX NAME)



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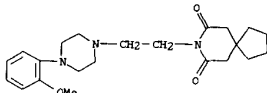


PAGE 2-A

RN 191592-08-2 CAPLUS

L14 ANSWER 107 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:430404 CAPLUS
DOCUMENT NUMBER: 127:134218
TITLE: In vivo electrophysiological characterization of
5-HT
receptors in the guinea pig head of caudate
nucleus
and orbitofrontal cortex
AUTHOR(S): Mansari, M. El; Blier, P.
CORPORATE SOURCE: Neurobiological Psychiatry Unit, McGill Univ.,
Montreal, QC, H3A 1A1, Can.
SOURCE: Neuropharmacology (1997), 36(4/5), 577-588
CODEN: NEUPHW; ISSN: 0028-3908
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The aim of the present study was to characterize in vivo the 5-HT
receptor
subtypes which mediate the effect of microiontophoretic applied 5-HT
in
the guinea pig head of caudate nucleus and orbitofrontal cortex.
5-HT and
the preferential 5-HT_{2A} receptor agonist DOI and the preferential
5-HT_{2C}
receptor agonist mCPP, suppressed the quisqualate (QUIS)-induced
activation of neurons in both structures. The inhibitory effect of
DOI
and mCPP was not prevented by acute i.v. administration of the 5-HT_{1/2}
receptor antagonist metergoline (2 mg/kg) and the 5-HT_{2A/2C} receptor
antagonist ritanserin (2 mg/kg) in the two regions nor by the
selective
5-HT_{2A} receptor antagonist MDL100907 (1 mg/kg) in the head of caudate
nucleus. However, the inhibitory effect of DOI, but not that of
mCPP, was
antagonized by a 4-day treatment with metergoline and ritanserin (2
mg/kg/day; using minipumps implaced s.c.) in the head of caudate
nucleus,
but not in the orbitofrontal cortex. Microiontophoretic ejection of
the
5-HT_{1A/7} receptor agonist 8-OH-DPAT and of the 5-HT_{1A} receptor
antagonist
WAY100635 both suppressed the spontaneous and QUIS-activated firing
activity of the orbitofrontal cortex neurons. At currents which did
not
affect the basal discharge activity of the neuron recorded,
microiontophoretic application of WAY100635 and BWY7378 failed to
prevent
the inhibitory effect of 8-OH-DPAT. The inhibitory effect of
geprone,
which is a 5-HT_{1A} receptor agonist but devoid of affinity for 5-HT₇
receptors, was also not antagonized by WAY100635. Altogether, these
results suggest the presence of atypical 5-HT_{1A} receptors in the
orbitofrontal cortex. The present results also indicate that the
suppressant effect of DOI may be mediated by 5-HT_{2A} receptors in the
head
of caudate nucleus and atypical 5-HT₂ receptors in the
orbitofunctional

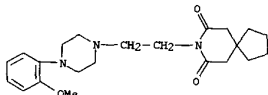
L14 ANSWER 107 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 IT 21102-95-4, BMY7378
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BIOL (Biological study)
 (characterization of 5-HT receptors in guinea pig head of caudate
 nucleus and orbitofrontal cortex in relation to obsessive
 compulsive disorder)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

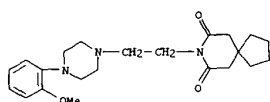
L14 ANSWER 108 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:406096 CAPLUS
 DOCUMENT NUMBER: 127:130790
 TITLE: .alpha.1-Adrenoceptor subtype selectivity:
 molecular modeling and theoretical quantitative
 structure-affinity relationships
 AUTHOR(S): De Benedetti, P. G.; Fanelli, F.; Menziani, M. C.;
 Cocchi, M.; Testa, R.; Leonardi, A.
 CORPORATE SOURCE: Dipartimento di Chimica, Universita di Modena,
 Modena, 41100, Italy
 SOURCE: Bioorganic & Medicinal Chemistry (1997), 5(5),
 809-816
 CODEN: BMECEP; ISSN: 0968-0896
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB This study constitutes a preliminary rationalization, at the mol.
 level, of antagonist selectivity towards the three cloned .alpha.1-adrenergic
 receptor (.alpha.1-AR) subtypes. Mol. dynamics simulations allowed a
 structural/dynamics anal. of the seven .alpha.-helix-bundle models of
 the bovine .alpha.1a-, hamster .alpha.1b-, and rat .alpha.1d-AR subtypes.
 The results showed that the transmembrane domains of these subtypes have
 different dynamic behaviors and different topogs. of the binding
 sites, which are mainly constituted by conserved residues. In particular,
 the .alpha.1a-AR binding site is more flexible and topog. different with
 respect to the other two subtypes. The results of the theor.
 structural/dynamics anal. of the isolated receptors are consistent
 with the binding affinities of the 16 antagonists tested towards the three
 cloned .alpha.1-AR subtypes. Moreover, the theor. quant.
 structure-affinity relationships obtained from the antagonist-receptor
 interaction models further corroborate the hypothesis that selectivity
 towards one preferential subtype is mainly modulated by receptor
 and/or ligand distortion energies. In other words, subtype selectivity
 seems to be mainly guided by the dynamic complementarity (induced fit) between
 ligand and receptor. On the basis of the quant. models presented it
 is possible to predict both affinities and selectivities of putative
 .alpha.1-AR ligands as well as to est. the theor. .alpha.1-AR subtype
 affinities and selectivities of existing antagonists.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (mol. modeling and QSAR of .alpha.1-Adrenoceptor subtype
 selectivity)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 108 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



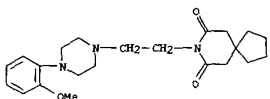
●2 HCl

L14 ANSWER 109 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:331431 CAPLUS
 DOCUMENT NUMBER: 127:60476
 TITLE: Analysis of .alpha.1-adrenoceptors in rabbit lower
 urinary tract and mesenteric artery
 AUTHOR(S): Van der Graaf, Pieter H.; Deplanne, Valerie;
 Duquenne, Chantal; Angel, Itzhak
 CORPORATE SOURCE: Syntheslabo Recherche (L.E.R.S.), Department of
 Internal Medicine, B.P. 248, 10 rue des Carrieres,
 Rueil Malmaison, 92500, Fr.
 SOURCE: European Journal of Pharmacology (1997), 327(1),
 25-32
 CODEN: EJPHAZ; ISSN: 0014-2999
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In this study, we have investigated the effects of a series of
 .alpha.1-adrenoceptor antagonists on the phenylephrine-mediated
 contractions of rabbit isolated prostate, urethra, trigone and
 mesenteric artery. With the exception of RS-17053 (N-[2-(2-
 cyclopropylmethoxyphenoxy)ethyl]-5-chloro-.alpha.,.alpha.-dimethyl-1H-
 indole-3-ethanamine hydrochloride), the antagonists displayed the
 lowest potency in the urethra. Catecholamine uptake1 and uptake2 appeared
 not to be the cause for the low pKB /pA2 values obtained in the urethra
 because cocaine and corticosterone had no effect on the potency of
 phenylephrine in this tissue. The low potencies displayed by prazosin, RS-17053 and
 HV723 (.alpha.-ethyl-3,4,5-trimethoxy-.alpha.-(3-((2-(2-
 methoxyphenoxy)ethyl)amino)propyl)benzene-acetonitrile fumarate)
 suggest that the functional receptors in all four tissues belong to the
 .alpha.1L-adrenoceptor class. Whether or not the significant
 between-tissue differences in antagonist potencies are due to
 heterogeneity of this receptor class remains to be elucidated.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); BIOL (Biological study)
 (pharmacol. characteristics of the .alpha.1-adrenoceptors in rabbit
 lower urinary tract and mesenteric artery)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 110 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
are not readily detectable at the protein level in a variety of rat tissues where their mRNA is expressed. The biphasic competition curves of some agonists and antagonists in chloroethyl-clonidine-treated rat tissues do not represent .alpha.1D-adrenoceptors and are not readily explained by the present .alpha.1A/.alpha.1B/.alpha.1D-adrenoceptor classification.
IT 21102-95-4, RMY 7378
RL: BFR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (investigations of presence of .alpha.1D-adrenoceptors in rat tissues at protein level)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

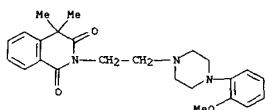


●2 HCl

L14 ANSWER 110 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:234024 CAPLUS
DOCUMENT NUMBER: 127:1136
TITLE: .alpha.1D-adrenoceptor protein detectable in rat tissues?
AUTHOR(S): Yang, Ming; Verfurth, Frank; Buscher, Rainer; Michel, Martin C.
CORPORATE SOURCE: Department Medicine, University Essen, Essen, Germany
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1997), 355(4), 438-446
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB We have used the .alpha.1D-adrenoceptor selective antagonist, RMY 7378, the .alpha.1D-selective agonists, adrenaline and phenylephrine, the .alpha.1A-selective antagonists, (+)-niquldipine, SB 216469 and WB4101, and the non-subtype-selective .alpha.1-adrenoceptor antagonist, nemonapride, to investigate the presence of .alpha.1D-adrenoceptors in rat tissues at the protein level. Radio-ligand binding studies using [3H]prazosin as the radio-ligand were performed in three tissues contg. .alpha.1D-adrenoceptor mRNA, spleen, cerebral cortex and kidney, and in comparison in one tissue not contg. .alpha.1D-adrenoceptor mRNA, liver. Cerebral cortex and kidney were also studied upon .alpha.1B-adrenoceptor inactivation by chloroethylclonidine treatment (10 .mu.M, 30 min, 37.degree.). Expts. with cloned rat .alpha.1-adrenoceptor subtypes transiently expressed in COS cells confirmed the known selectivity of the investigated drugs for .alpha.1-adrenoceptor subtypes or the lack thereof of nemonapride. Accordingly nemonapride had steep and monophasic competition curves in all native and chloroethylclonidine-treated tissues. RMY 7378 also had steep and monophasic competition curves and low affinity in all native tissues. In contrast, adrenaline and phenylephrine (in the presence of 100 .mu.M GTP) had monophasic competition curves of low affinity in liver and spleen but biphasic competition curves in cerebral cortex and kidney. Following chloro-ethylclonidine treatment competition curves for adrenaline, phenylephrine, (+)-niquldipine, SB 216469 and WB 4101 remained biphasic in cerebral cortex and kidney while those for nemonapride remained monophasic. We conclude that .alpha.1D-adrenoceptors

L14 ANSWER 111 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:220142 CAPLUS
DOCUMENT NUMBER: 127:76453
TITLE: .alpha.2C-adrenoceptors mediate contractile responses to noradrenaline in the human saphenous vein
AUTHOR(S): Gavin, K. T.; Colgan, M. P.; Moore, D.; Shanik, G.; Docherty, J. R.
CORPORATE SOURCE: Department Physiology, Royal College Surgeons, Dublin, Ire.
SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (1997), 355(3), 406-411
CODEN: NSAPCC; ISSN: 0028-1298
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Postjunctional .alpha.2-adrenoceptors in the saphenous vein were investigated for the ability of .alpha.2-adrenoceptor antagonists to shift the contractile potency of noradrenaline. The following antagonists were employed: chlorpromazine, BDF 8933, prazosin, ARC 239, yohimbine, HV 723, WB 4101, SKF 104078, and BRL 44408. Antagonist potency at postjunctional .alpha.2-adrenoceptors was correlated with antagonist affinity at .alpha.2-adrenoceptor ligand binding sites in membranes of human platelet (.alpha.2), rat kidney (.alpha.2B) and Sf 9 cells expressing human recombinant receptors (.alpha.2C). The correlation with the postjunctional .alpha.2-adrenoceptor mediating contraction of the saphenous vein was best for the human recombinant .alpha.2C-adrenoceptor ligand binding site, as compared to correlations with the .alpha.2B-adrenoceptor ligand binding site of rat kidney and with the .alpha.2A-adrenoceptor ligand binding site of human platelet. It is concluded that the functional postjunctional .alpha.2-adrenoceptor mediating contractions of the saphenous vein closely resembles the human recombinant .alpha.2C-adrenoceptor ligand binding site.
IT 67339-62-2, ARC 239
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (affinity of, at the .alpha.2-adrenoceptor ligand binding sites in human platelet, rat kidney, human recombinant receptors and potencies in saphenous vein)
RN 67339-62-2 CAPLUS
CN 1,3-(2H,4H)-isouquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 111 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

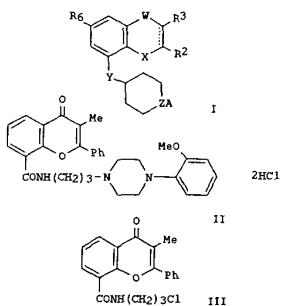


L14 ANSWER 112 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:169157 CAPLUS
DOCUMENT NUMBER: 126:225315
TITLE: Bicyclic heterocyclic derivatives having
.alpha.1-adrenergic and 5HT1A serotonergic
activities
INVENTOR(S): Leonardi, Amedeo; Motta, Gianni; Riva, Carlo;
Testa, Rodolfo
PATENT ASSIGNEE(S): Recordati S.A., Chemical and Pharmaceutical
Company, Switz.
SOURCE: U.S., 84 pp., Cont.-in-part of U.S. 5,474,994.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

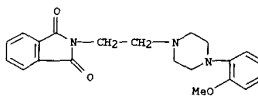
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|------|-------------------|-----------------|-------------|
| US 5605896 | A | 19970225 | US 1994-299188 | 19940831 |
| US 5403842 | A | 19950404 | US 1992-888775 | 19920526 |
| AU 9336296 | A1 | 19930913 | AU 1993-36296 | 19930223 |
| RO 1121111 | B3 | 19970530 | RO 1994-1404 | 19930223 |
| PL 175556 | B1 | 19990129 | PL 1993-304889 | 19930223 |
| RU 2128656 | C1 | 19990410 | RU 1994-43324 | 19930223 |
| SK 280143 | B6 | 19990910 | SK 1994-1007 | 19930223 |
| ZA 9301278 | A | 19931118 | ZA 1993-1278 | 19930224 |
| LT 3038 | B | 19940925 | LT 1993-354 | 19930224 |
| CN 1079738 | A | 19931222 | CN 1993-105852 | 19930526 |
| CN 1040434 | B | 19981028 | | |
| US 5474994 | A | 19951212 | US 1993-67861 | 19930526 |
| FI 9403876 | A | 19940823 | FI 1994-3876 | 19940823 |
| NO 9403140 | A | 19940823 | NO 1994-3140 | 19940825 |
| PRIORITY APPL. INFO.: | | | IT 1992-MI408 | A 19920225 |
| | | | US 1992-888775 | A2 19920526 |
| | | | US 1993-67861 | A2 19930526 |
| | | | EP 1993-301264 | A 19930222 |
| | | | WO 1993-EP420 | A 19930222 |
| OTHER SOURCE(S): | | MARFAT 126:225315 | | |
| GI | | | | |

L14 ANSWER 112 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 112 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

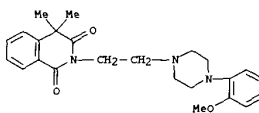
(Reactant or reagent)
(prepn. of bicyclic heterocyclic derivs. having
.alpha.1-adrenergic and
5HT1A serotonergic activities)
RN 99718-67-9 CAPLUS
CN 1H-Indole-1,3(2H)-dione,
2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)



AB Bicyclic heterocyclic derivs., such as I [X = N, O, S; W = C(O),
C(S),
CH(OH), bond; R2 = H, optionally substituted alkyl, alkenyl,
alkynyl,
carbocycle, heterocycle; R3 = alkyl, hydroxyalkyl, Ph, OH, alkoxy,
alkoxyalkyl; R6 = H, halogen, NO2, NH2, AcNH, mono-, dialkylamino,
CN, OH,
alkoxy, alkyl; Y = CO, CO2, CONH, CH(OH), CH:CH, CH:CHCO2, CH:CHCONH,
CH2NH, CH2NHCO, CH2NH5O2, CH2O, CH2S, NH, NHCO, NHCONH, NH5O2, O, S,
SO2NH, CONHO, CSNH, NHCO2, CO5, CONH(CH2)m, m = 1-6; Z = N, A =
(un)substituted Ph, pyrimidinyl, 1,4-benzodioxan-8-yl,
benzopyran-8-yl,
benzofuran-7-yl, dihydrobenzopyran-8-yl; Z = CH2N; Z = CH, A = one
or two
Ph, 4-FC6H4CO, 2-oxo-1-benzimidazolyl, (CH2)nOAc, n = 0-2], and
their
pharmaceutically acceptable salts useful as .alpha.1-adrenergic and
5HT1A
serotonergic agents for the treatment of hypertension, urethral and
lower
urinary tract contractions, and other disorders are described. Thus,
benzopyran II was prepd. by heating 1-(2-methoxyphenyl)piperazine
with
benzopyran III at 180.degree. for 5 h. II had IC50 = 29 nM for
.alpha.1-adrenergic receptor binding, IC50 = 9 nM for 5HT1A receptor
binding, ED25 = 45 .mu.g/kg i.v. hypotensive effect and ED25 = 1.4
.mu.g/kg in Na-induced urethral contractility assays.
IT 99718-67-9P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);
RACT

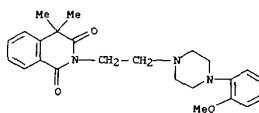
L14 ANSWER 113 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:88411 CAPLUS
 DOCUMENT NUMBER: 126:259093
 TITLE: [3H]2-(2-benzofuranyl)-2-imidazoline, a highly selective radioligand for I2-imidazoline receptor binding sites. Studies in rabbit kidney membranes
 AUTHOR(S): Moeseni, A. R.; King, P. R.; Louis, W. J.;
 Gundlach,
 CORPORATE SOURCE: A. L. Austin Repatriation Med. Cent., University Melbourne,
 SOURCE: Austin, Australia
 (1997), Naunyn-Schmiedeberg's Archives of Pharmacology
 PUBLISHER: 355(1), 131-138
 DOCUMENT TYPE: CODEN: NSAPCC; ISSN: 0028-1298
 LANGUAGE: English
 AB 2-(2-Benzofuranyl)-2-imidazoline (2-BFI) has recently been characterized as a selective ligand for the I2-type of imidazoline-receptor binding site(s) (I2-RBS). The present studies detd. the relative levels of specific [3H]2-BFI binding to membrane homogenates of brain and kidney from rat, guinea pig and rabbit and identified the pharmacol. characteristics of [3H]2-BFI binding sites in rabbit kidney membranes. Rabbit kidney membranes had the highest relative d. of specific [3H]2-BFI binding of all tissues studied (2000 fmol/mg protein). Rabbit brain and guinea pig kidney had moderate levels of specific [3H]2-BFI binding (350500 fmol/mg protein), while rat kidney and guinea pig and rat brain displayed much lower densities of binding (4065 fmol/mg protein). Studies of [3H]2-BFI binding kinetics in rabbit kidney homogenates revealed binding to two distinct sites with Kd values of 0.10 nmol/l and 1.00 nmol/l resp. Drug inhibition studies revealed that L-adrenaline, .alpha.1-adrenoceptor drugs (prazosin, L-phenylephrine) and .alpha.2-adrenoceptor drugs (rauwolscine, methoxyidazoxan, ARC-239) had extremely low affinities for [3H]2-BFI binding sites (IC50 .gtoreq. 10 .mu.mol/l). Putative I1-RBS compds., p-aminoclonidine, moxonidine, imidazole-4-acetic acid and cimetidine, inhibited [3H]2-BFI binding to rabbit renal membranes with low to very low affinities (Ki values 3 to .gtoreq. 100 .mu.mol/l), suggesting [3H]2-BFI does not label I1-RBS in rabbit kidney membranes. I2-RBS compds.BU224, BU239, idazoxan, and cirazoline inhibited [3H]2-BFI binding confirming the labeling of I2-RBS. Inhibition of [3H]2-BFI binding by certain compds. was consistent with

L14 ANSWER 113 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 their interaction with two binding site populations for example (drug, Ki values) guanabenz, 0.65 nmol/l and 0.17 .mu.mol/l; naphazoline, 0.94 nmol/l and 2.8 .mu.mol/l; amiloride, 76 nmol/l and 26 .mu.mol/l rilmenidine, 150 nmol/l and 50 .mu.mol/l; and clonidine, 230 nmol/l and 70 pmol/l. These results demonstrate that [3H]2-BFI is a highly selective and high affinity radioligand for I2-RBS which should be useful for the further characterization of these sites in mammalian tissues.
 IT 67339-62-2, ARC-239
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) ([3H]2-(2-benzofuranyl)-2-imidazoline, a highly selective radioligand for I2-imidazoline receptor binding sites in rabbit kidney and brain)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



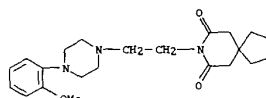
L14 ANSWER 114 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:70999 CAPLUS
 DOCUMENT NUMBER: 126:113098
 TITLE: Investigation of the subtype of .alpha.2-adrenoceptor mediating pressor responses in the pithed rat
 AUTHOR(S): Gavin, Katherine; Docherty, James R.
 CORPORATE SOURCE: Dep. Physiol., Royal Coll. Surgeons Ireland, Dublin,
 SOURCE: Ire. European Journal of Pharmacology (1996), 318(1), 81-87
 PUBLISHER: CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Elsevier
 LANGUAGE: English
 AB We have investigated the subtype of .alpha.2-adrenoceptor mediating postjunctional pressor responses in the pithed rat in comparison with .alpha.2-adrenoceptor ligand binding sites. In pithed rats, postjunctional .alpha.2-adrenoceptors were investigated in terms of the ability of .alpha.2-adrenoceptor antagonists to shift the pressor potency of the .alpha.2-adrenoceptor agonist xylazine. Antagonist potency at postjunctional .alpha.2-adrenoceptors in the pithed rat was correlated with antagonist affinity at .alpha.2-adrenoceptor ligand binding sites in membranes of rat kidney (.alpha.2B), Sf9 cells expressing human recombinant receptors (.alpha.2C) and rat submandibular gland (.alpha.2D) labeled with [3H]yohimbine. The correlation with the postjunctional .alpha.2-adrenoceptor mediating pressor responses in the pithed rat was better for the .alpha.2D-adrenoceptor ligand binding site of rat submandibular gland (r = 0.95) and the .alpha.2B-adrenoceptor ligand binding site of rat kidney (r = 0.90) than with the human recombinant .alpha.2C-adrenoceptor ligand binding site (r = 0.81). When the pressor potencies of three addnl. antagonists were included in the correlations for .alpha.2B- and .alpha.2D-sites only, the correlation with .alpha.2D-adrenoceptor ligand binding site of rat submandibular gland (r = 0.91) was much better than with the .alpha.2B-adrenoceptor ligand binding site of rat kidney (r = 0.77). It is concluded that the functional postjunctional .alpha.2-adrenoceptors mediating pressor responses in the pithed rat most closely resemble the .alpha.2D-adrenoceptors subtype.
 IT 67339-62-2, ARC 239
 RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 PROC (Process)
 pithed (subtype of .alpha.2-adrenoceptor mediating pressor responses in

L14 ANSWER 114 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 rat in comparison with ligand binding sites)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



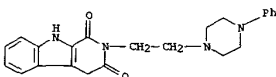
L14 ANSWER 115 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:743484 CAPLUS
 DOCUMENT NUMBER: 126:152648
 TITLE: Reduction of guinea pig pup isolation calls by anxiolytic and antidepressant drugs
 AUTHOR(S): Molewijk, H. E.; Hartog, K.; Van Der Poel, A. M.; Mos, J.; Olivier, B.
 CORPORATE SOURCE: CNS Pharmacology, Solvay Duphar B. V., Weesp, 1380 DA, Neth.
 SOURCE: Psychopharmacology (Berlin) (1996), 128(1), 31-38
 PUBLISHER: CODEN: PSCHDL; ISSN: 0033-3158
 DOCUMENT TYPE: Springer
 LANGUAGE: Journal
 AB Guinea pigs possess central 5-HT1D receptors similar to humans but different from rats and mice. The effects of a variety of psychotropic drugs on guinea pig pup isolation calls was assessed. Anxiolytic compds. such as the benzodiazepine receptor agonists diazepam and alprazolam, the full 5-HT1A receptor agonists 8-OH-DPAT and flesinoxan, and also reduced isolation calling by the guinea pig pup. Moreover, mixed antidepressant/anxiolytic compds. like the 5-HT uptake inhibitors fluvoxamine and clomipramine or the MAO-inhibitor clorgyline as well as the antidepressant NA uptake inhibitors desipramine and maprotiline suppressed vocalizations. The 5-HT1D/1A receptor agonist 5-CT was also very effective in reducing sepn. calls. Remarkably, the partial 5-HT1A receptor agonists buspirone and BMV 7378 did not affect calling. The neuroleptic haloperidol, the psychostimulant d-amphetamine, the putative anxiogenics DMCM and m-CPP and the putative anxiolytics ondansetron and CI-988 had no effect on isolation calls of guinea pig pups. This paradigm could be helpful to assess behavioral effects of anxiolytic and antidepressant drugs in a species different from rat or mouse, and in which the effects of 5-HT1D receptor ligands may possibly be established.
 IT 21102-95-4, BMV 7378
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USBS (Uses)
 (redn. of guinea pig pup isolation calls by anxiolytic and antidepressant drugs)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 115 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

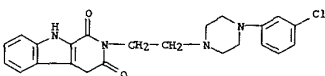


● 2 HCl

L14 ANSWER 116 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:731716 CAPLUS
 DOCUMENT NUMBER: 126:31237
 TITLE: 4-Aryl-1-piperazinylalkyl derivatives of 1,2,3,4-tetrahydro-beta-carboline ring system. Synthesis and preliminary in vivo studies
 AUTHOR(S): Cegla, Marek T.; Boksa, J.; Chojnacka-Wojcik, E.; Misztal, S.
 CORPORATE SOURCE: Collegium Medicum, Jagiellonian University, Krakow, 30688, Pol.
 SOURCE: Pharmazie (1996), 51(12), 932-936
 PUBLISHER: CODEN: PHARAT; ISSN: 0031-7144
 DOCUMENT TYPE: Govi-Verlag Pharmazeutischer Verlag
 LANGUAGE: Journal
 AB Three series of compds. contg. a 4-aryl-1-piperazinylalkyl fragment attached to different positions of indole or 1,2,3,4-tetrahydro-beta-carboline were prepd. A quant. relationship between the structure of some deriva. and their sedative effect was found using the Free-Wilson approach.
 IT 184691-40-5P 184691-41-6P 184691-42-8P
 184691-44-9P 184691-51-8P 184691-52-9P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (prepn., sedative effect, antiserotonin activity, and QSAR of (arylpiperazinylalkyl)tetrahydrocarbolines)
 RN 184691-40-5 CAPLUS
 CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 4,9-dihydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

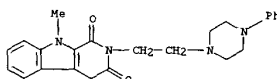


RN 184691-41-6 CAPLUS
 CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-4,9-dihydro- (9CI) (CA INDEX NAME)

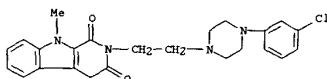


L14 ANSWER 116 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

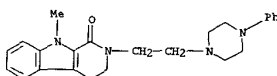
RN 184691-43-8 CAPLUS
 CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 4,9-dihydro-9-methyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



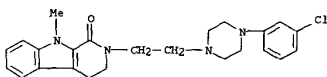
RN 184691-44-9 CAPLUS
 CN 1H-Pyrido[3,4-b]indole-1,3(2H)-dione, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-4,9-dihydro-9-methyl- (9CI) (CA INDEX NAME)



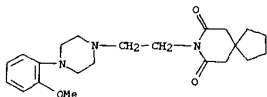
RN 184691-51-8 CAPLUS
 CN 1H-Pyrido[3,4-b]indol-1-one, 2,3,4,9-tetrahydro-9-methyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 184691-52-9 CAPLUS
 CN 1H-Pyrido[3,4-b]indol-1-one, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-2,3,4,9-tetrahydro-9-methyl- (9CI) (CA INDEX NAME)

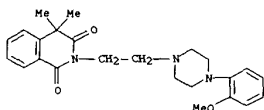


L14 ANSWER 117 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:673359 CAPLUS
 DOCUMENT NUMBER: 125:318433
 TITLE: Pharmacological evidence that different .alpha.1 adrenoceptor subtypes mediate contraction in rabbit prostate and hypogastric artery
 AUTHOR(S): Delafiotte, S.; Auguet, M.; Chabrier, P. E.
 CORPORATE SOURCE: Institut Henri Beaufour Research Labs., Les Ulis, Fr.
 SOURCE: Acta Physiologica Scandinavica (1996), 158(3), 241-251
 CODEN: AFSCAX; ISSN: 0001-6772
 PUBLISHER: Blackwell
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The .alpha.1-adrenoceptor subtypes mediating contraction of rabbit prostate and hypogastric artery were pharmacol. characterized using an isolated organ bath technique. The prostate had the same sensitivity to the contractile action of methoxamine and phenylephrine, whereas the hypogastric artery was five times less sensitive to the action of methoxamine in comparison with phenylephrine. Clonidine elicited contraction in the hypogastric artery but not in the prostate.
 BMJ7378 was about 70-fold more potent to antagonize the phenylephrine-induced contraction in the hypogastric artery (pA₂, 8.14) than in the prostate (pA₂ 6.28), and 5-methyl-urapidil was about three-fold more potent on prostate than on hypogastric artery. The potency of different .alpha.1-adrenoceptor antagonists tested in the rabbit prostate was significantly correlated with their binding affinity for the expressed recombinant .alpha.1A-, but no .alpha.1B- or .alpha.1D-, adrenoceptor subtype, whereas, the potency of the .alpha.1-adrenoceptor antagonists tested in the rabbit hypogastric artery was better correlated with the defined .alpha.1D-adrenoceptor. Chloroethylclonidine produced a 10-fold rightward shift in the phenylephrine concn.-response curve in the hypogastric artery but only had a weak effect in the prostate. The results indicates that significant heterogeneity exists among .alpha.1-adrenoceptor in the rabbit hypogastric artery (.alpha.1D-adrenoceptor) and the prostate (.alpha.1A-adrenoceptor).
 IT 21102-95-4 CAPLUS
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (pharmacol. evidence that different .alpha.1 adrenoceptor subtypes mediate contraction in rabbit prostate and hypogastric artery)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



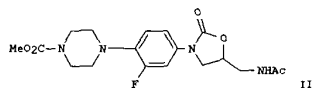
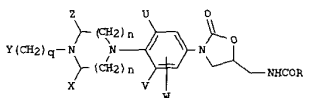
● 2 HCl

L14 ANSWER 118 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:595110 CAPLUS
 DOCUMENT NUMBER: 125:318251
 TITLE: The subtype-selective .alpha.2-adrenoceptor antagonists BRL 44408 and ARC 239 also recognize 5-HT1A receptors in the rat brain
 AUTHOR(S): Mesna, J. Javier; Callado, Luis F.; Pazos, Angel; Grijalba, Bernardo; Garcia-Sevilla, Jesus A.
 CORPORATE SOURCE: Department of Pharmacology, University of the Basque Country, E-48940, Leioa, Spain
 SOURCE: European Journal of Pharmacology (1996), 312(3), 385-388
 CODEN: EJPHAZ; ISSN: 0014-2999
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Several .alpha.2-adrenoceptor compds. have been reported to recognize 5-HT1A receptors. The interaction of the .alpha.2A/D- and .alpha.2B/C-adrenoceptor antagonists BRL 44408 (2-[2H-(1-methyl-1,3-dihydroisindol-4-yl)-4,5-dihydroimidazole] and ARC 239 (2-[2-[4-(o-methoxyphenyl)piperazin-1-yl]ethyl]-4,4-dimethyl-1,3-(2H,4H)-isoquinolinedione) with 5-HT1A receptors was evaluated in rat brain. Competition expts. in cortex with both compds. against the specific binding of the 5-HT1A receptor radioligand [3H]8-OH-DPAT (8-hydroxy-2-(n-dipropyl-amine)-tetralin) yielded K_i values in the nanomolar range, fairly close to their previously reported affinities for .alpha.2-adrenoceptors. Similar K_i values were obtained under .alpha.2-adrenoceptor masking conditions by competition assays of these compds. against the .alpha.2-adrenoceptor and 5-HT1A receptor radioligand [3H]RX #21002 (2-methoxy idazoxan) specific binding in hippocampus. The results indicate that BRL 44408 and ARC 239 recognize 5-HT1A receptors in addn. to .alpha.2-adrenoceptors. The fact should be considered when using these compds. to study .alpha.2-adrenoceptor subtypes.
 IT 67339-62-2, Arc239
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (subtype-selective .alpha.2-adrenoceptor antagonists BRL 44408 and ARC 239 recognize 5-HT1A receptors in rat brain)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 119 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:537790 CAPLUS
 DOCUMENT NUMBER: 125:221870
 TITLE: (Piperazinylphenyl)oxazolidinone antimicrobials
 INVENTOR(S): Hutchinson, Douglas K.; Barbachyn, Michael R.;
 Brickner, Steven J.; Gammill, Ronald E.; Patel,
 Mahesh
 V.
 PATENT ASSIGNEE(S): Upjohn Co., USA
 SOURCE: U.S., 19 pp., Cont.-in-part of U.S. Ser. No. 880,
 432,
 abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|-------------------|-----------------|-------------|
| US 5547950 | A | 19960820 | US 1994-332822 | 19941031 |
| HU 72296 | A2 | 19960429 | HU 1994-3208 | 19930421 |
| CZ 281884 | B6 | 19970312 | CZ 1994-2505 | 19930421 |
| ZA 9302855 | A | 19941024 | ZA 1993-2855 | 19930422 |
| IL 105555 | A1 | 19980715 | IL 1993-10555 | 19930423 |
| CN 1079964 | A | 19931229 | CN 1993-105039 | 19930508 |
| CN 1044236 | B | 19990721 | | |
| US 5700799 | A | 19971223 | US 1996-610031 | 19960304 |
| PRIORITY APPLN. INFO.: | | | US 1992-880432 | B2 19920508 |
| | | | US 1994-332822 | A3 19941031 |
| OTHER SOURCE(S): | | MARPAT 125:221870 | | |
| G1 | | | | |



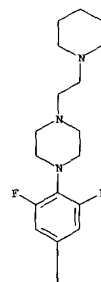
AB Title compds. I or pharmaceutically acceptable salts thereof wherein:
 each

L14 ANSWER 119 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 n is independently 1 to 3; Y is chosen from, e.g., (a) C(O)C1-6
 alkyl,
 C(O)OC1-6 alkyl or benzoyl, (b) N(R3)2 where R3 is independently
 hydrogen,
 C1-4 alkyl or Ph which can be substituted with one to three F, Cl,
 OCH3,
 CH, NH2, or C1-4 alkyl, wherein each occurrence of said C1-6 alkyl
 may be
 substituted with one or more F, Cl, Br, I, OR1, CO2R1, CN, SR1, or R1
 (where R1 is a hydrogen or C1-4 alkyl); X and Z are independently
 C1-6
 alkyl, C3-12 cycloalkyl or hydrogen, or X and Z form a C0-3 bridging
 group, preferably X and Z are hydrogen; U, V and W are independently
 C1-6
 alkyl, F, Cl, Br, hydrogen or a C1-6 alkyl substituted with one or
 more of
 F, Cl, Br or I, preferably U and V are F and W is hydrogen; R is
 hydrogen,
 C1-12 alkyl, C3-12 cycloalkyl, C1-6 alkoxy, C1-6 alkyl substituted
 with
 one or more F, Cl, Br, I or OH; and q is 0 to 4 inclusive, are useful
 antimicrobial agents, effective against a no. of human and veterinary
 pathogens, including multiply-resistant staphylococci and
 streptococci, as
 well as anaerobic organisms such as bacteroides and clostridia
 species,
 and acid-fast organisms such as Mycobacterium tuberculosis and
 Mycobacterium avium. Thus, e.g., arylation of piperazine with
 3,4-difluoronitrobenzene afforded
 1-(2-fluoro-4-nitrophenyl)piperazine;
 Boc protection followed by redn. provided
 1-(tert-butoxycarbonyl)-4-(2-
 fluoro-4-aminophenyl)piperazine; the latter was converted to the CHz
 deriv. and then allylated to give
 1-(tert-butoxycarbonyl)-4-(2-fluoro-4-
 benzyloxycarbonylallylamino)piperazine; dihydroxylation followed by
 cyclization afforded 3-[3-fluoro-4-(4-tert-butoxycarbonylpiperazin-1-
 yl)phenyl]-5-hydroxymethyl-2-oxazolidinone; the 5-hydroxymethyl
 group was
 converted to a 5-acetylaminoethyl group by mesylation,
 azidification,
 hydrogenation, and acetylation; finally, Boc deprotection followed by
 treatment with MeO2CCl afforded oxazolidinone II which exhibited
 antibacterial activity ED50 of 1.8 mg/kg PO against S. aureus vs. 1.8
 mg/kg SC for vancomycin, and 2.3 mg/kg PO against S. pyogenes vs. 2.6
 mg/kg SC for clindamycin.
 IT 154590-81-SR 154590-90-6P
 RL: RAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
 use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 ((piperazinylphenyl)oxazolidinone antimicrobials)
 RN 154590-81-5 CAPLUS
 CN Acetamide, N-[[3-[3,5-difluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-
 piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-, (S)- (9CI) (CA
 INDEX

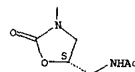
L14 ANSWER 119 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 NAME)

Absolute stereochemistry.

PAGE 1-A



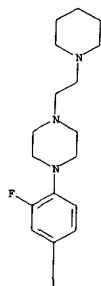
PAGE 2-A



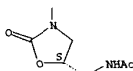
RN 154590-90-6 CAPLUS
 CN Acetamide, N-[[3-[3-fluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-
 piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-, (S)- (9CI) (CA
 INDEX
 NAME)

Absolute stereochemistry.

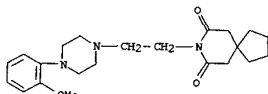
PAGE 1-A



PAGE 2-A

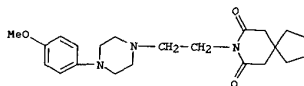


L14 ANSWER 120 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



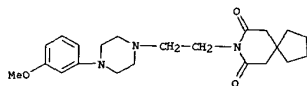
● 2 HC1

RN 25024-76-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HC1

RN 179388-69-3 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

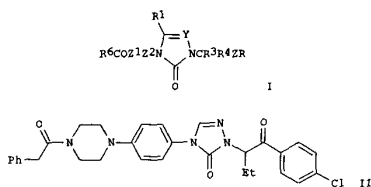


● 2 HC1

L14 ANSWER 120 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:435300 CAPLUS
 DOCUMENT NUMBER: 125:104287
 TITLE: Structure activity relationships of a series of buspirone analogs at alpha-1 adrenoceptors:
 further evidence that rat aorta alpha-1 adrenoceptors are of the alpha-1D-subtype
 AUTHOR(S): Saussy, David L., Jr.; Goetz, Aaron S.; Queen, Kennedy L.; King, Holly K.; Lutz, Michael W.; Rimele, Thomas J.
 CORPORATE SOURCE: Dep. Receptor Biochem., Glaxo Wellcome, Inc., Research Triangle Park, NC, USA
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1996), 278(1), 136-144
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: Williams & Wilkins
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The activity of a series of buspirone analogs at recombinant and rat thoracic aorta alpha-1 adrenoceptors was investigated. Compd. affinity for recombinant alpha-1A, alpha-1B and alpha-1D adrenoceptors from human and animal sources was detd. by radioligand binding assays using membranes prep'd. from rat-1 fibroblasts expressing recombinant receptors with (+/-)-[125I]iodo-HEAT as the radioligand. Compd. affinity and functional activity at rat aortic alpha-1 adrenoceptors were detd. using endothelium denuded rings contracted with phenylephrine. BMJ 7378 and MDL 73005EF were found to have significant selectivity for the alpha-1D-subtype and were high affinity antagonists of the alpha-1 adrenoceptors in the rat aorta. Leverage plot anal. of affinities of the buspirone analogs and a series of structurally diverse alpha-1 antagonists for recombinant alpha-1 adrenoceptors and rat aorta alpha-1 adrenoceptors demonstrate that the alpha-1 adrenoceptors in the rat aorta are predominantly of the alpha-1D subtype.
 IT 21102-95-4, BMJ 7378 25024-76-4 179388-69-3
 RI: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
 (structure activity relationships of buspirone analogs at .alpha.1-adrenoceptors and characterization of rat aorta .alpha.1-adrenoceptors as .alpha.1D subtype)
 RN 21102-95-4 CAPLUS

L14 ANSWER 121 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:252231 CAPLUS
 DOCUMENT NUMBER: 124:289578
 TITLE: Preparation of N-[(4-(alkanoyl- and aroyl)piperazinopyridyl)triazolones and analogs as anti-Helicobacter agents
 INVENTOR(S): Heeres, Jan; Stokbroek, Raymond Antoine; Hostmans, Joseph Hector; Van Der Veken, Louis Jozef Elis
 PATENT ASSIGNEE(S): Janssen Pharmaceutica N.V., Belg.
 SOURCE: PCT Int. Appl., 27 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|------------|
| WO 9601822 | A1 | 19960125 | WO 1995-EP2618 | 19950705 |
| W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SG, SI, SK, TJ, TT, UA, UG, US, UZ, VN | | | | |
| RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, EF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5637592 | A | 19970610 | US 1995-448082 | 19950523 |
| CA 2193490 | AA | 19960125 | CA 1995-2193490 | 19950705 |
| AU 9530757 | A1 | 19960209 | AU 1995-30757 | 19950705 |
| AU 685310 | B2 | 19980115 | | |
| EP 770074 | A1 | 19970502 | EP 1995-926392 | 19950705 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE | | | | |
| CN 1152311 | A | 19970618 | CN 1995-194023 | 19950705 |
| CN 1071331 | B | 20010919 | | |
| BR 9508377 | A | 19971028 | BR 1995-8377 | 19950705 |
| HU 76638 | A2 | 19971028 | HU 1997-76 | 19950705 |
| JP 10502385 | T2 | 19980303 | JP 1995-504111 | 19950705 |
| RU 2152392 | C1 | 20000710 | RU 1997-102153 | 19950705 |
| ZA 9505759 | A | 19970113 | ZA 1995-5759 | 19950711 |
| IL 114536 | A1 | 19990411 | IL 1995-114536 | 19950711 |
| NO 9700088 | A | 19970310 | NO 1997-88 | 19970109 |
| FI 9700112 | A | 19970110 | FI 1997-112 | 19970110 |
| PRIORITY APPLN. INFO.: | | | EP 1994-202019 | A 19940712 |
| | | | WO 1995-EP2618 | W 19950705 |
| OTHER SOURCE(S): | | | MARPAT 124:289578 | |
| GI | | | | |



AB Title compds. [I; R = (un)substituted Ph; R1-R3 = H, alkyl; R6 = (cyclo)alkyl, (hetero)aryl, etc.; Y = CH or N; Z = CO, CH(OH); Z1 = piperazine-1,4-di-yl; Z2 = 1,4-phenylene, pyridine-2,5-di-yl, pyrimidine-2,5-di-yl] were prep'd. Thus, title comp'd. II had MIC of .1 to req. 1. mu.M against *Helicobacter pylori* in vitro.

IT 175715-52-3P 175715-53-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);

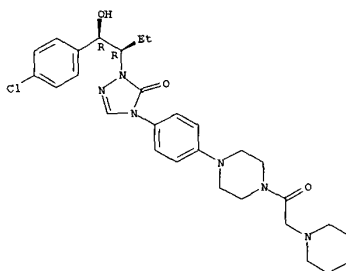
BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of N-[(4-(alkanoyl- and aroyl)piperazinyl)pyridyl]triazolones and analogs as anti-*Helicobacter* agents)

RN 175715-52-3 CAPLUS

CN Piperazine,

1-[4-[1-[1-[(4-chlorophenyl)hydroxymethyl]propyl]-1,5-dihydro-5-oxo-4H-1,2,4-triazol-4-yl]phenyl]-4-(1-piperidinylacetyl)-, (R*,R*)- (9CI) (CA INDEX NAME)

Relative stereochemistry.

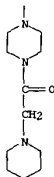
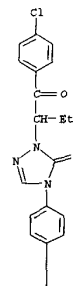


RN 175715-53-4 CAPLUS

CN Piperazine,

1-[4-[1-[1-(4-chlorobenzoyl)propyl]-1,5-dihydro-5-oxo-4H-1,2,4-triazol-4-yl]phenyl]-4-(1-piperidinylacetyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



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ACCESSION NUMBER: 1996:190223 CAPLUS

DOCUMENT NUMBER: 124:306503

TITLE: 2-[4-[4-(4-methoxyphenyl)piperazin-1-ylmethyl]-1,3-dioxoperhydroimidazo[1,5-a]pyridine as a new selective 5-HT1A receptor ligand

AUTHOR(S): Lopez-Rodriguez, Maria L.; Morcillo, M. Jose; Rosado, M. Luisa; Benhamu, Bellinda; Sanz, Antonio M. Fac. Ciencias Quimicas, Univ. Complutense, Madrid, 28040, Spain

CORPORATE SOURCE: Bioorg. Med. Chem. Lett. (1996), 6(6), 689-94

SOURCE: CODEN: BMCLE#; ISSN: 0960-894X

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 124:306503

AB A series of 2-[omega-(4-arylpiperazin-1-yl)alkyl]-1,3-dioxoperhydroimidazo[1,5-a]pyridine derivs. was prep'd. and evaluated

for affinity at 5-HT1A and .alpha.1 receptors. The most promising analog

bound at 5-HT1A sites with nanomolar affinity (Ki = 31.7) and high

selectivity over .alpha.1, D2 and 5-HT2.alpha. receptors (Ki > 1000,

Ki > 10 000, Ki > 1000 nM, resp.). Preliminary studies showed that this

agent is a presynaptic 5-HT1A agonist, and it displayed activity in the

face to face behavioral model.

IT 21102-94-3

RL: BPR (Biological process); FRP (Properties); BIOL (Biological study);

PROC (Process)

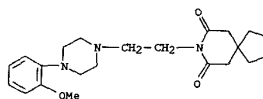
(prepn. of dioxoperhydroimidazopyridine derivs. as new selective

serotonergic 51A receptor ligands in relation to agonist

activity and structure)

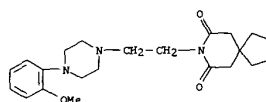
RN 21102-94-3 CAPLUS

CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



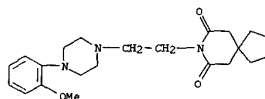
L14 ANSWER 123 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:95589 CAPLUS
 DOCUMENT NUMBER: 124:232163
 TITLE: 8-[4-[2-(1,2,3,4-Tetrahydroisoquinolinyl)]butyl]-8-azaspiro[4.5]decane-7,9-dione: A New 5-HT1A Receptor
 Ligand with the Same Activity Profile as
 Buspirone
 AUTHOR(S): Mokrosz, Jerzy L.; Deren-Wesolek, Anna; Tatarczyńska, Ewa; Duszyńska, Beata; Bojarski, Andrzej J.; Mokrosz, Maris J.; Chojnacka-Wojcik, Ewa
 CORPORATE SOURCE: Institute of Pharmacology, Polish Academy of Sciences, Krakow, 31-343, Pol.
 SOURCE: Journal of Medicinal Chemistry (1996), 39(5), 1126-9
 CODEN: JMCHAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A new analog of buspirone, i.e., 8-[4-[2-(1,2,3,4-tetrahydroisoquinolinyl)]butyl]-8-azaspiro[4.5]decane-7,9-dione (6a), was synthesized. It was demonstrated that buspirone and its analog 6a were equipotent 5-HT1A ligands. Several behavioral models showed that 6a had essentially the same functional profile at 5-HT1A receptors as buspirone. The obtained results permit a conclusion that the basic nitrogen atom and terminal, bulky cycloimide moiety, but not the 2-pyrimidinyl group, of buspirone are directly involved in the formation of the bioactive complex with 5-HT1A receptors.
 IT 21102-94-3
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (activity as a 5-HT1A receptor ligand)
 RN 21102-94-3 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 123 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 124 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1996:18915 CAPLUS
 DOCUMENT NUMBER: 124:46391
 TITLE: The specific contribution of the novel alpha-1D adrenoceptor to the contraction of vascular smooth muscle
 AUTHOR(S): Flascik, Michael T.; Guarino, Richard D.; Smith, Marta S.; Soltis, Edward E.; Saussy, David L., Jr.; Perez, Dianne M.
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Kentucky, Lexington, KY, USA
 SOURCE: Journal of Pharmacology and Experimental Therapeutics (1995), 275(3), 1583-8
 CODEN: JPETAB; ISSN: 0022-3565
 PUBLISHER: Williams & Wilkins
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB With a selective antagonist, the specific contribution of the alpha-1D adrenoceptor (AR) to vascular smooth muscle contraction has been assessed. BMY 7378 bound to membranes expressing the cloned rat alpha-1D AR with a >100-fold higher affinity (K1 = 2 nM) than binding to either the cloned rat alpha-1A AR (K1 = 800 nM) or the hamster alpha-1B AR (K1 = 600 nM). BMY 7378 exhibited differential potency in inhibiting vascular smooth muscle contraction. In the rat aorta and iliac artery, BMY 7378 was a high-affinity antagonist, producing parallel shifts in the phenylephrine concn.-response curve. The disocn. consts. for this compd. by Schild anal. were 0.95 and 4 nM for the aorta and iliac artery, resp. The slopes of these Schild plots were not significantly different from unity. BMY 7378 was a weak antagonist in the rat caudal, mesenteric resistance and renal arteries, with Schild slopes significantly <1. With RNase protection assays, alpha-1D mRNA was found in all blood vessels examd. These data suggest that (1) BMY 7378 is a selective alpha-1D AR antagonist that can be used in functional systems to assess the contribution of this receptor in vascular smooth muscle contraction; (2) the alpha-1D AR appears to play a major role in the contraction of the aorta and iliac artery; (3) despite the fact that the mRNA for the alpha-1D AR can be detected in the caudal, mesenteric resistance and renal arteries, it does

L14 ANSWER 124 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 not appear to play a role in mediating contraction of these blood vessels; and (4) expression of alpha-1D mRNA in a particular artery does not ensure that this receptor is involved in regulating the contraction of that artery.
 IT 21102-95-4, BMY 7378
 RL: RUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (.alpha.1D-adrenoceptor-mediated vascular smooth muscle contraction antagonism by BMY 7378)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

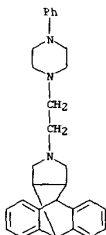
L14 ANSWER 125 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:916470 CAPLUS
 DOCUMENT NUMBER: 123:314021
 TITLE: Preparation of piperazine-substituted pyrroloanthracenes as immunomodulators.
 INVENTOR(S): Schwenner, Eckhard; Ladouceur, Gaeton; Kabbe, Hans-Joachim; Aune, Thomas Martin
 PATENT ASSIGNEE(S): Bayer A.-G., Germany
 SOURCE: PCT Int. Appl., 74 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9515946 | A1 | 19950615 | WO 1994-EP3934 | 19941128 |
| W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, UA, VN | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 5409932 | A | 19950425 | US 1993-164499 | 19931209 |
| US 5459143 | A | 19951017 | US 1993-164509 | 19931209 |
| AU 9512411 | A1 | 19950627 | AU 1995-12411 | 19941128 |
| EP 733040 | A1 | 19960925 | EP 1995-903294 | 19941128 |
| R: CH, DE, FR, GB, IT, LI | | | | |
| JP 09506356 | T2 | 19970624 | JP 1994-515934 | 19941128 |
| PRIORITY APPLN. INFO.: US 1993-164499 19931209 | | | | |
| US 1993-164509 19931209 | | | | |
| WO 1994-EP3934 19941128 | | | | |
| OTHER SOURCE(S): MARPAT 123:314021 | | | | |
| GI | | | | |

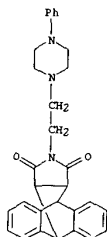
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. (I), A, D = H, OH, halo, cyano, CO₂H, NO₂, CF₃, OCF₃, alkyl, alkoxy; R₁, R₂ = H, halo, cyano, CHO, Ph, OH, (substituted) alkyl, alkenyl; R₅, R₆ = H, halo, Ph, (substituted) alkyl; R₇-R₁₀ = H, alkyl; R₇R₈, R₉R₁₀ = O; a = 2-8; R₁₁ = H, cycloalkyl, pyridyl, pyrimidinyl, (substituted) aryl, alkyl, were prepd. Thus, 9,10-dihydro-9,10[3',4']-furananthracene-12,14(11H,15H)-dione (prepn. given) was refluxed with 3-(4-(4-fluorophenyl)piperazin-1-yl)propylamine (prepn. given) in xylene using a water separator to give 98% title compd. (II). At 10 mg/kg i.p. in rats, I gave 4-90% inhibition of paw swelling in the adjuvant arthritis

L14 ANSWER 125 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



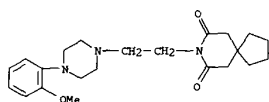
L14 ANSWER 125 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 model.
 IT 169877-38-7P 169877-92-3P
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of piperazine-substituted pyrroloanthracenes as immunomodulators)
 RN 169877-38-7 CAPLUS
 CN 4,9[1',2']-Benzeno-1H-benz[f]isindole-1,3(2H)-dione, 3a,4,9,9a-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 169877-92-3 CAPLUS
 CN 4,9[1',2']-Benzeno-1H-benz[f]isindole, 2,3,3a,4,9,9a-hexahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

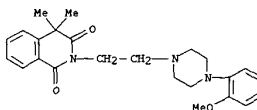
L14 ANSWER 126 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:882567 CAPLUS
 DOCUMENT NUMBER: 123:329777
 TITLE: Effects of the NMDA antagonist, dizocilpine, in various drug discriminations: characterization of intermediate levels of drug lever selection
 AUTHOR(S): Koek, W.; Kleven, M.S.; Colpaert, F.C.
 CORPORATE SOURCE: Centre de Recherche Pierre Fabre, Castres, 81106, Fr.
 SOURCE: Behav. Pharmacol. (1995), Volume Date 1995, 6(5 & 6), 590-600
 CODEN: BPHAEI; ISSN: 0955-8810
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In each of different groups of rats trained to discriminate either 8-OH-DPAT, DOI, d-amphetamine, cocaine, chlordiazepoxide, or ethanol from saline, dizocilpine produced max. percentages of drug lever (DL) selection that were intermediate between those produced by the training conditions. Dizocilpine also decreased DL selection produced by the training dose in each of the discriminations, except in ethanol-trained rats. In all discriminations, with the exception of ethanol-trained rats, the intermediate levels of DL selection produced by dizocilpine were assocd. with increased FRF values (sum of the responses made on either lever before the first reinforcement occurred), increased lever selection latencies, and increased responding on the nonselected lever. At doses that, in general, had effects on response rate similar to those of dizocilpine, intermediate levels of DL selection were produced by BMY 7378 in 8-OH-DPAT-trained rats, by WY 50,324 in DOI-trained rats, by (-)-3-PPP in d-amphetamine- and in cocaine-trained rats, by alpidem in chlordiazepoxide-trained rats, and by PCP in ethanol-trained rats. The intermediate levels of DL selection produced by these latter drugs were not assocd. with simultaneous increases of FRF values, selection latencies, and responding on the nonselected lever. The results suggest that dizocilpine produces intermediate levels of drug-appropriate responding through the behavioral mechanism of partial generalization only in ethanol-trained rats; in all other discriminations examd. here, the effects of dizocilpine appear to involve (1) pharmacol. effects that differ from those of the training drug, and (2) behavioral mechanisms that are unrelated to stimulus generalization. The differentiation of partial generalization and other mechanisms whereby intermediate responding can occur in the drug discrimination paradigm requires analyses that are more

L14 ANSWER 126 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 detailed than those commonly used in drug discrimination research.
 IT 21102-95-4, RMY 7378
 RL: BAC (Biological activity or effector, except adverse); BIOL
 (Biological study)
 (effects of the NMDA antagonist, dizocilpine, in various drug
 discriminations; characterization of intermediate levels of drug
 lever selection)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



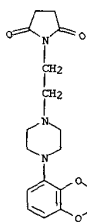
●2 HCl

L14 ANSWER 127 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:828929 CAPLUS
 DOCUMENT NUMBER: 123:275756
 TITLE: Identification of drugs subtype-selective for
 .alpha.2A-, .alpha.2B-, and
 .alpha.2C-adrenoceptors in
 the pig cerebellum and kidney cortex
 AUTHOR(S): Wikberg-Matsson, Anna; Wikberg, Jarl E. S.; Uhlen,
 Staffan
 CORPORATE SOURCE: Department of Ophthalmology, Academic Hospital,
 Uppsala, Swed.
 SOURCE: Eur. J. Pharmacol. (1995), 284(3), 271-9
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The radioligands [3H]MK912 and [3H]RX821002 were used to label
 .alpha.2A-,
 .alpha.2B-, and .alpha.2C-adrenoceptors of the pig cerebellum and
 kidney
 cortex. By inclusion of the .alpha.2A-adrenoceptor-selective drug,
 BRI44408, and using a 'multi-curve' exptl. design all the three
 porcine
 .alpha.2-adrenoceptor subtypes could be characterized pharmacol. The
 data
 indicate that the pig .alpha.2-adrenoceptor subtypes are pharmacol.
 more
 related to human .alpha.2-adrenoceptor subtypes than to the rodent
 .alpha.2-adrenoceptors. The authors suggest a set of drugs that are
 useful for the delineation of the pig .alpha.2-adrenoceptor subtypes.
 IT 67339-62-2, ARC239
 RL: RFR (Biological process); BIOL (Biological study); PROC (Process)
 (identification of drugs subtype-selective for .alpha.2A-,
 .alpha.2B-,
 and .alpha.2C-adrenoceptors in the pig cerebellum and kidney
 cortex)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

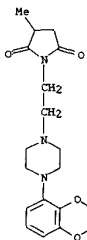


L14 ANSWER 128 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:826862 CAPLUS
 DOCUMENT NUMBER: 124:55875
 TITLE: A Series of N4-Imidoethyl Derivatives of
 1-(2,3-Dihydro-1,4-benzodioxin-5-yl)piperazine as
 5-HT1A Receptor Ligands: Synthesis and
 Structure-Affinity Relationships
 AUTHOR(S): van Steen, B. J.; van Wijngaarden, I.; Tulp, M.
 Th.
 CORPORATE SOURCE: M.; Soudijn, W.
 Department of Medicinal Chemistry, Solvay Duphar
 Research Laboratories, Weesp, 1380 DA, Neth.
 SOURCE: Journal of Medicinal Chemistry (1995), 38(21),
 4303-8
 CODEN: JMCHAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A series of unsubstituted and substituted succinimido, maleimido, and
 glutarimidoethyl derivs. of eltopazine was synthesized and tested
 for
 affinity for the 5-HT1A receptor in rat brain homogenates. The
 unsubstituted compds. have a moderate affinity for the receptor,
 while the
 affinity considerably increases by substitution at or enlargement of
 these
 cyclic ring systems. A good correlation was found between the
 inhibition
 const. Ki (expressed as pKi) and the lipophilicity (clogP). No
 correlation was obsd. between the pKi or pKi+ (local inhibition
 const.)
 and the basicity of the N4-nitrogen atom.
 IT 171877-00-2P 171877-01-3P 171877-02-4P
 171877-03-5P 171877-08-0P 171877-09-1P
 171877-10-4P 171877-11-5P 171877-13-7P
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
 use);
 BIOL (Biological study); PREF (Preparation); USES (Uses)
 (synthesis and structure-affinity relationships of N4-imidoethyl
 derivs. of (Dihydrobenzodioxinyl)piperazine)
 RN 171877-00-2 CAPLUS
 CN 2,5-Pyrrolidinedione, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

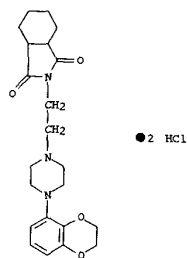
L14 ANSWER 128 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



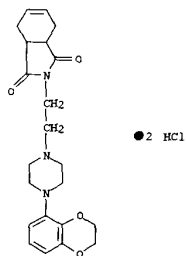
RN 171877-01-3 CAPLUS
 CN 2,5-Pyrrolidinedione, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-
 piperazinyl]ethyl]-3-methyl- (9CI) (CA INDEX NAME)



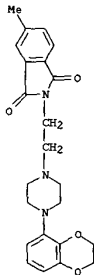
RN 171877-02-4 CAPLUS
 CN 1H-Indole-1,3(2H)-dione,
 2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-
 piperazinyl]ethyl]hexahydro-, dihydrochloride (9CI) (CA INDEX NAME)



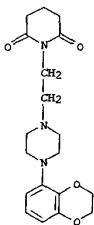
RN 171877-03-5 CAPLUS
 CN 1H-Isindole-1,3(2H)-dione,
 2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-
 piperazinyl]ethyl]-3a,4,7,7a-tetrahydro-, dihydrochloride (9CI) (CA
 INDEX NAME)



RN 171877-08-0 CAPLUS
 CN 1H-Isindole-1,3(2H)-dione,
 2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-



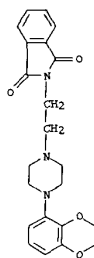
RN 171877-10-4 CAPLUS
 CN 2,6-Piperidinedione, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 171877-11-5 CAPLUS
 CN 2,6-Piperidinedione, 1-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-
 piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX
 NAME)

CM 1

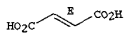
CRN 171877-07-9
 CMF C22 H23 N3 O4



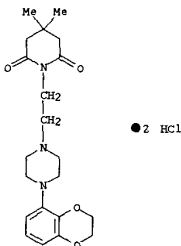
CM 2

CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.



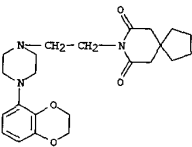
RN 171877-09-1 CAPLUS
 CN 1H-Isindole-1,3(2H)-dione,
 2-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-yl)-1-
 piperazinyl]ethyl]-5-methyl- (9CI) (CA INDEX NAME)



RN 171877-13-7 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione,
 8-[2-[4-(2,3-dihydro-1,4-benzodioxin-5-
 yl)-1-piperazinyl]ethyl]-, mono(4-methylbenzenesulfonate) (9CI) (CA
 INDEX NAME)

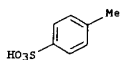
CM 1

CRN 171877-12-6
 CMF C23 H31 N3 O4

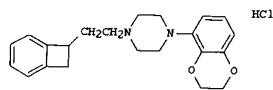


CM 2

CRN 104-15-4
 CMF C7 H8 O3 S

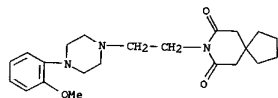


L14 ANSWER 129 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:790900 CAPLUS
 DOCUMENT NUMBER: 124:134742
 TITLE: Characterization of Potent and Selective Antagonists at Postsynaptic 5-HT1A Receptors in a Series of N4-Substituted Arylpiperazines
 AUTHOR(S): Paglioni, Jean-Louis; Canton, Hervé; Bervoets, Alain;
 Karim;
 Audinot, Valerie; Brocco, Maurice; Gobert, Le Marouille-Girardon, Sylvie; Millan, Mark J.
 CORPORATE SOURCE: Institut de Recherches Servier, Suresnes, 92150, Fr.
 SOURCE: Journal of Medicinal Chemistry (1995), 38(20), 4044-55
 PUBLISHER: CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: American Chemical Society
 LANGUAGE: Journal
 GI: English



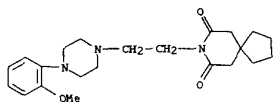
AB Benzocycloalkyl and benzocycloalkenyl moieties linked, directly or via an alkyl chain, to oxygen-bearing heteroarylpiperazines were synthesized, in an attempt to obtain potent and selective antagonists at postsynaptic 5-HT1A receptors. From the numerous arylpiperazines described in the literature, 1-(2,3-dihydro-1,4-benzodioxin-5-yl)piperazine was chosen as a model of an arylpiperazine in view of its selectivity for 5-HT1A receptors vs. .alpha.1-, .alpha.2-, and .beta.-adrenergic receptors, as well as dopamine D1 and D2 receptors. Two other closely-related arylpiperazines, 1-(1,5-benzodioxepin-6-yl)piperazine and 1-(benzofuran-7-yl)piperazine, were also examined in this study. All compounds showed high affinity at 5-HT1A sites (8.10 .ltoreq. pKis < 9.35), and the majority behaved as antagonists in vivo in blocking the hypothermia induced by the 5-HT1A agonist 8-OH-DPAT in the absence of a marked effect alone at equivalent doses. An in vivo evaluation of dopamine D2 receptor antagonist properties revealed that the majority of compounds was devoid of activity at this site,

L14 ANSWER 129 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 in marked contrast to RMY 7378 which displayed virtually no selectivity for 5-HT1A vs. dopamine D2 receptors. Moreover, six compounds of the present series, including I, showed >10-fold selectivity in vitro for 5-HT1A vs. .alpha.1-adrenergic receptors. I displayed an optimal compromise between potency (pKi = 8.75), marked antagonist activity, and selectivity toward .alpha.1-adrenergic (81-fold) and dopamine D2 195-fold receptors. These characteristics clearly distinguish I from previously-reported ligands such as the postsynaptic 5-HT1A antagonist RMY 7378 and the weak partial agonist NAN 190 which, in contrast to the compounds of this series, belong to the well-exemplified class of imido derivatives of (o-methoxyphenyl)piperazines. The availability of I (S 15535) should facilitate the further elucidation of the functional role and potential therapeutic significance of 5-HT1A receptors.
 IT 21102-95-4, RMY 7378
 RL: RAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (potent and selective antagonists at postsynaptic 5-HT1A receptors in a series of N4-substituted arylpiperazines)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 130 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:698387 CAPLUS
 DOCUMENT NUMBER: 123:103264
 TITLE: Studies on the role of 5-HT1A autoreceptors and alpha.1-adrenoceptors in the inhibition of 5-HT release. I. RMY 7378 and prazosin
 AUTHOR(S): Hjorth, S.; Bengtsson, H. J.; Milano, S.;
 Lundberg, J.
 CORPORATE SOURCE: F.; Sharp, T.
 413 90, Dep. Pharmacology, Univ. Goeteborg, Goeteborg, Swed.
 SOURCE: Neuropharmacology (1995), 34(6), 615-20
 CODEN: NEPHEW; ISSN: 0028-3908
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The present study utilized in vivo microdialysis to investigate the importance of 5-HT1A autoreceptors and .alpha.1-adrenoceptors in the decreased 5-HT release obtained following administration of the mixed 5-HT1A autoreceptor partial agonist/.alpha.1-adrenoceptor antagonist RMY 7378, the selective 5-HT1A receptor agonist 8-OH-DPAT and the .alpha.1-adrenoceptor antagonist prazosin. RMY 7378 (0.25 mg/kg, s.c.), 8-OH-DPAT (0.025 mg/kg, s.c.) and prazosin (0.1-1.0 mg/kg, s.c.) all suppressed ventral hippocampal 5-HT efflux. The RMY 7378- and 8-OH-DPAT-induced inhibition of 5-HT release were reversed by a 40 min pretreatment with either (+/-)pindolol (8 mg/kg, s.c.) or WAY-100635 (0.3 mg/kg, s.c.), to block 5-HT1A autoreceptors. Neither of these antagonists altered the prazosin-induced (0.3 mg/kg, s.c.) 5-HT decrease. The results: (i) confirm that both an .alpha.1-adrenoceptor antagonist (prazosin) and 5-HT1A autoreceptor stimulants (RMY 7378 and 8-OH-DPAT) may reduce cerebral 5-HT release; (ii) support that the RMY 7378-induced decrease in 5-HT release results from 5-HT1A autoreceptor agonism, rather than .alpha.1-adrenoceptor blockade; and (iii) argue against "physiol." antagonism (i.e. via blockade of .beta.-adrenoceptors, 5-HT1B receptors or some other mechanism) as an explanation for the reversal by pindolol of 5-HT1A autoreceptor agonist-induced suppression of 5-HT release. These data support the usefulness of pindolol, as well as the more specific compound WAY-100635, to block 5-HT1A autoreceptors.
 IT 21102-95-4, RMY 7378
 RL: RAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (5-HT1A autoreceptors and .alpha.1-adrenoceptors in inhibition of hippocampal 5-HT release)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 131 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

greatest sensitivity. Drug potency for inhibition of firing and turnover was highly correlated ($r = 0.80-0.82$) and these actions were significantly correlated to affinity at (hippocampal) 5-HT_{1A} receptors ($r = 0.62-0.73$).

As concerns DA D₂ autoreceptors, the agonist action of apomorphine in reducing DA turnover were mimicked only by 8-OH-DPAT, whereas the majority of the other 5-HT_{1A} ligands, in analogy to raclopride, enhanced DA turnover. The facilitation of DA turnover appeared to reflect direct blockage of DA D₂ autoreceptors because potency was correlated powerfully to affinity at these D₂ sites ($r = 0.83$). None of the 5-HT_{1A} ligands mimicked the agonist action of clonidine at alpha-2 AR autoreceptors, whereas the turnover-enhancing actions of the alpha-2 AR antagonists, idazoxan and 1-(2-pyrimidinyl)piperazine, were mimicked by many 5-HT_{1A} ligands. Their potency did not, however, correlate with their affinity at alpha-2 ARs ($r = 0.13$), probably because the alpha-2 AR antagonist actions of several ligands reflect their metab. to 1-(2-pyrimidinyl)piperazine.

In conclusion, in addn. to their agonist or antagonist actions at central 5-HT_{1A} autoreceptors, many 5-HT_{1A} ligands display pronounced in vivo actions at presynaptic DA D₂ receptors and alpha-2 ARs.

Nevertheless, several ligand, such as S 14671, (+)-flesinoxan, S 15535 and WAY 100,235, display marked selectivity for 5-HT_{1A} autoreceptors and an evaluation of their potential therapeutic properties should prove of particular interest.

IT 21102-95-4, RMY 7378

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BIOL (Biological study); PROC (Process)

(modulation of the activity of central serotonergic neurons by novel serotonin1A receptor agonists and antagonists)

RN 21102-95-4 CAPLUS

CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 131 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1995:644351 CAPLUS

DOCUMENT NUMBER: 123:26183

TITLE: Modulation of the activity of central serotonergic neurons by novel serotonin1A receptor agonists and antagonists: a comparison to adrenergic and dopaminergic neurons in rats

AUTHOR(S): Gobert, A.; Lejeune, F.; Rivet, J.-M.; Audinot, V.;

CORPORATE SOURCE: Newman-Tancredi, A.; Millan, M. J. Dep. of Psychopharmacology, Inst. Recherches Servier, Croissy-sur-Seine, 78290, Fr.

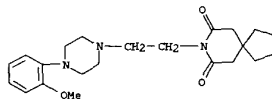
SOURCE: J. Pharmacol. Exp. Ther. (1995), 273(3), 1032-46

CODEN: JFETAB; ISSN: 0022-3565

DOCUMENT TYPE: Journal

LANGUAGE: English

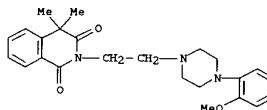
AB In this study, the authors used a complementary in vivo electrophysiol. and (in individual rats) neurochem. approach to characterize the actions of chem. diverse serotonin (5-HT)_{1A} receptor ligands at central 5-HT_{1A} autoreceptors as compared to dopamine (DA) D₂ autoreceptors and presynaptic alpha-2 adrenergic receptors (ARs). The novel, high efficacy, 5-HT_{1A} agonists, WY 48,723 (an arylpiperazine), (+)-flesinoxan (a benzodioxane) and S 14671 and S 14506 (methoxynaphthylpiperazines) mimicked the aminotetralin, 8-hydroxy-2-(di-n-propylamino)tetralin hydrobromide (8-OH-DPAT), in inhibiting the firing of dorsal raphe nucleus (DRN) neurons. Similarly, the firing rate of DRN neurons was reduced by the "partial" agonists, MDL 73005EF, RMY 7378, NAN-190, tandospirone and the novel pyrimidinylpiperazine, zalcospirone. Furthermore, S 14489, S 15535 and S 15931, novel benzodioxopiperazines, which behave as antagonists at postsynaptic 5-HT_{1A} receptors, inhibited completely DRN firing, whereas the methoxyphenylpiperazine, WAY 100,135, and the arylalkylamine, (-)-tertadolol, were ineffective. Indeed, in analogy to spiperone, both WAY 100,135 and (-)-tertadolol behaved as apparently competitive antagonists in that, in their presence, the dose-response curves for inhibition of DRN firing by S 14671, S 14506 or 8-OH-DPAT were shifted in parallel to the right with no loss of maximal effect. In distinction to WAY 100,135 and (-)-tertadolol, a further novel, putative "antagonist," SDZ 216-525 (a benzoisothiazolpiperazine) weakly inhibited the elec. activity of the DRN. With the exception of (-)-tertadolol, which behaved as a weak agonist, a very similar pattern of inhibition of 5-HT turnover was seen in the striatum (innervated by the DRN), the hippocampus and the hypothalamus (DRN and median raphe nucleus) and the spinal cord (nucleus raphe magnus), with the striatum displaying the



●2 HCl

L14 ANSWER 132 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:622064 CAPLUS
 DOCUMENT NUMBER: 123:47330
 TITLE: Comparison of the binding activities of some drugs on .alpha.2A, .alpha.2B and .alpha.2C-adrenoceptors and non-adrenergic imidazoline sites in the guinea pig
 AUTHOR(S): Uhlen, Staffan; Muceniece, Ruta; Rangel, Winfa; Tiger, Gunnar; Wikberg, Jarl E. S.
 CORPORATE SOURCE: Dep. Pharmacology, Umea Univ., Umea, S-901 87, Swed.
 SOURCE: Pharmacol. Toxicol. (Copenhagen) (1995), 76(6), 353-64
 CODEN: PHTOEH; ISSN: 0901-9928
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Simultaneous computer modeling of control and guanfacine-masked [3H]-MK 912 satn. curves as well as guanfacine competition curves revealed that both .alpha.2A- and .alpha.2C-adrenoceptor subtypes were present in the guinea pig cerebral cortex. The Kd value of [3H]-MK 912 detd. for the .alpha.2A-subtype was 403 pM and for the .alpha.2C-subtype 79.8 pM; the receptor sites showing capacities 172 and 19.5 fmol/mg protein, resp. The Kds of guanfacine were 20 and 880 nM for the .alpha.2A- and .alpha.2C-adrenoceptor, resp. In the guinea pig kidney [3H]-MK 912 bound to a single saturable site with Kd 8.34 nM and capacity 285 fmol/mg protein, the site showing pharmacol. properties like an .alpha.2B-adrenoceptor. Binding consts. of 22 compds. for the three guinea pig .alpha.2-adrenoceptor subtypes were detd. by computer modeling competition curves using for the cerebral cortex a "3-curve assay", for the kidney an "1-curve assay", and using [3H]-MK 912 as labeled ligand. Of the tested drugs guanfacine and BRL 4408 were found to be clearly .alpha.2A-selective. Spiroaxatine, yohimbine, rauwolfscine and Wb 4101, as well as [3H]-MK 912 itself, were found to be .alpha.2C-selective. The most selective compds. for .alpha.2B-adrenoceptors, when compared to .alpha.2A-adrenoceptors, were ARC 239 and prazosin. In the guinea pig kidney [3H]-p-aminoclonidine bound to .alpha.2-adrenoceptors as well as to non-adrenergic imidazoline sites. The .alpha.2-adrenoceptors could be completely blocked using 10 .mu.M (-)-adrenaline without the non-adrenergic sites being affected. During these conditions the anal. of

L14 ANSWER 132 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 combined satn. and competition studies using labeled and unlabeled p-aminoclonidine with computer modeling revealed that the ligand labeled two different sites with Kds of 310 and 47,000 nM, resp. Competition curves of 16 compds. for the non-adrenergic [3H]-p-aminoclonidine sites were shallow and resolved into two-site fits. For the high affinity [3H]-p-aminoclonidine site the highest affinities were shown by 1-medetomidine, UK-14,304, guanabenz and detomidine; the Kds of these drugs ranging 26-72 nM. All drugs tested showed low but varying affinities for the low affinity [3H]-p-aminoclonidine site. These data indicated that the [3H]-p-aminoclonidine binding sites of the guinea pig kidney are grossly different from the [3H]-idazoxan binding I2-receptors previously demonstrated also to be present in the guinea pig kidney. IT 67339-62-2, ARC 239
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (comparison of drug binding on .alpha.2A, .alpha.2B and .alpha.2C-adrenoceptors and non-adrenergic imidazoline sites in guinea pig)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

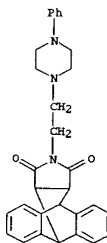


L14 ANSWER 133 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:604026 CAPLUS
 DOCUMENT NUMBER: 123:314014
 TITLE: Preparation of antiinflammatory 13-(piperazinyl)-9,10[3',4']pyrroloanthracene immunomodulators
 INVENTOR(S): Schwenner, Eckhard; Ladouceur, Gaetan; Kabbe, Hans-Joachim; Aune, Thomas M.
 PATENT ASSIGNEE(S): Bayer A.-G., Germany
 SOURCE: U.S., 16 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| US 5409932 | A | 19950425 | US 1993-164499 | 19931209 |
| WO 9515946 | A1 | 19950615 | WO 1994-EP3934 | 19941128 |

W: AU, BB, BG, BR, BY, CA, CN, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SI, SK, UA, VN
 RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
 AU 9512411 A1 19950627 AU 1995-12411 19941128
 EP 733040 A1 19960925 EP 1995-903294 19941128
 R: CH, DE, FR, GB, IT, LI
 JP 09506356 T2 19970624 JP 1994-515934 19941128
 PRIORITY APPLM. INFO.: US 1993-164499 19931209
 US 1993-164509 19931209
 WO 1994-EP3934 19941128
 OTHER SOURCE(S): MARPAT 123:314014
 GI

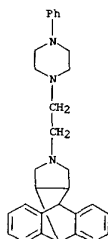
L14 ANSWER 133 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of antiinflammatory 13-(piperazinyl)-9,10[3',4']pyrroloanthracene immunomodulators)
 RN 169877-38-7 CAPLUS
 CN 4,9[1',2']-Benzeno-1H-benz[f]isoindole-1,3(2H)-dione, 2a,4,9,9a-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



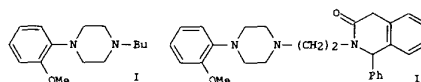
RN 169877-92-3 CAPLUS
 CN 4,9[1',2']-Benzeno-1H-benz[f]isoindole, 2,3,3a,4,9,9a-hexahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I: A, D = H, OH, halogen, CN, CO2H, NO2, CF3, CF3O, (un)branched C.ltoreq.8 alkyl or alkoxy; R1, R2 = H, halogen, CN, CHO, Ph, CH, (un)substituted alkoxy, (un)substituted alkyl, (un)substituted alkenyl; R3, R4 = H, C.ltoreq.6 (un)branched alkyl; R5, R6 = H, halogen, Ph, (un)branched (un)substituted alkyl; R7-R10 = H, C.ltoreq.6 (un)branched alkyl; R11 = (un)substituted aryl; a = 0-6] (e.g., II), useful as antiinflammatories, antiarthritics, and immunosuppressants, are prepd. Thus, II, m.p. 143.degree., was prepd. and demonstrated 90% inhibition of swelling in an adjuvant arthritis rat model at 10 mg/kg (i.p.).
 IT 169877-38-7p 169877-92-3p
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic)

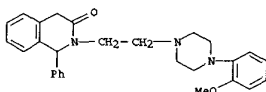


L14 ANSWER 134 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:540324 CAPLUS
 DOCUMENT NUMBER: 123:74214
 TITLE: Structure-activity relationship studies of CNS agents.
 AUTHOR(S): XXI: Two derivatives of 1-(o-methoxyphenyl)piperazine with an opposite function at 5-HT1A receptors
 AUTHOR(S): Mokrosz, Jerzy L.; Kłodzinska, Aleksandra; Boksa, Jan;
 CORPORATE SOURCE: Bojarski, Andrzej J.; Duszyńska, Beata; Chojnacka-Wojcik, Ewa
 Pharmacology, Dep. Med. Chem., Lab. New Drugs Inst.
 SOURCE: Polish Acad. Sci., Krakow, 31-343, Pol.
 Arch. Pharm. (Weinheim, Ger.) (1995), 328(4), 381-3
 CODEN: ARPMAS; ISSN: 0365-6233
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



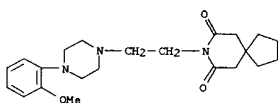
AB All postsynaptic 5-HT1A receptor antagonists which belong to the 1-aryl-piperazine class of ligands have a 1-(o-methoxyphenyl)piperazine fragment or its structural equiv. (e.g. benzodioxane moiety) in their structure. Mol. modeling and structure activity studies were conducted by using model compds. I and II to substantiate the hypothesis that 1-(o-methoxyphenyl)piperazine moiety is necessary for the 5-HT1A receptor antagonist activity. Comparison of the 5-HT1A/5-HT2A selective ratio for I and II shows that the structure of the bioactive complex of I with 5-HT1A receptors is different from the 5-HT1A receptor complex of II. The 1-Ph, and not the 1-(o-methoxyphenyl), substituent and the N-4 piperazine atom of II form a pharmacophore which is recognized by the receptor. It may be anticipated that the structure of the specific bioactive complex of 5-HT1A receptor and 1-(o-methoxyphenyl)piperazine fragment is directly responsible for postsynaptic antagonist activity of these derivs.
 IT 164988-55-0P
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

L14 ANSWER 134 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 (mol. modeling and structure activity relations of the 5-HT1A receptor antagonist (methoxyphenyl)piperazine derivs.)
 RN 164988-55-0 CAPLUS
 CN 3(2H)-isoquinolinone, 1,4-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-1-phenyl- (9CI) (CA INDEX NAME)



L14 ANSWER 135 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:470103 CAPLUS
 DOCUMENT NUMBER: 122:230666
 TITLE: Conditioned ultrasonic distress vocalizations in adult male rats as a behavioral paradigm for screening anti-panic drugs
 AUTHOR(S): Molewijk, H. E.; van der Poel, A. M.; Mos, J.; van der Heyden, J. A. M.; Olivier, B.
 CORPORATE SOURCE: CNS Pharmacol., Solvay Duphar B.V., Weesp, 1380 DA, Neth.
 SOURCE: Psychopharmacology (Berlin) (1995), 117(1), 32-40
 CODEN: PSCHDL; ISSN: 0033-3158
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Rats may produce ultrasonic vocalizations (USV) in threatening situations. USV of adult male rats in assocn. with aversive stimulation was evaluated as a screening method for anxiolytic drugs. The triazolobenzodiazepine alprazolam, the 5-HT uptake inhibitors fluvoxamine and clomipramine, the mixed 5-HT/NA uptake inhibitor imipramine, the full 5-HT1A receptor agonists 8-OH-DPAT and flesinoxan, the partial 5-HT1A receptor agonists buspirone, ipsapirone and RMY 7378, the .alpha.2-adrenoceptor agonist clonidine and the .alpha.2-adrenoceptor antagonist yohimbine reduced conditioned USV. The classical benzodiazepines (BZD) diazepam and chlordiazepoxide were ineffective or had a very low potency to decrease USV. The partial BZD receptor agonists bretazenil, alpidem and zolpidem, the BZD receptor antagonist flumazenil, the NA uptake inhibitors desipramine and maprotiline, and the 5-HT3 receptor antagonist ondansetron had no effect on conditioned USV. The dopamine-D2 receptor antagonist haloperidol reduced USV at a very high dose. In sep. expts. the effects of these drugs on locomotor activity were assessed. There was, however, no direct relation between effects on motor behavior and USV. In conclusion, the sensitivity of conditioned USV to 5-HT uptake inhibitors and alprazolam vs. the insensitivity to classical benzodiazepines and NA uptake inhibitors provides a very interesting profile, which closely resembles the psychopharmacol. of panic disorder. Also the face validity of conditioned USV towards situational panic attacks is high. We therefore propose conditioned USV in adult male rats as a novel behavioral paradigm to screen for anti-panic drugs.
 IT 21102-95-4, RMY 7378
 RL: BAC (Biological activity or effector, except adverse); THU

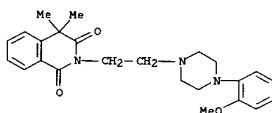
L14 ANSWER 135 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (conditioned ultrasonic distress vocalizations in adult male rats
 as a behavioral paradigm for screening antipanic drugs)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

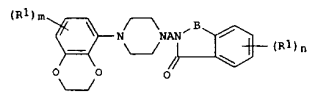
L14 ANSWER 136 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:466931 CAPLUS
 DOCUMENT NUMBER: 122:230657
 TITLE: Pharmacological antagonism of .alpha.-adrenergic agonist induced increases in canine intraurethral pressure in vivo
 AUTHOR(S): Brune, Michael E.; Buckner, Steven A.; Polakowski, James; Kerwin, James F., Jr.; Hancock, Arthur A. Pharmaceutical Products Division, Abbott
 CORPORATE SOURCE: Laboratories,
 SOURCE: Abbott Park, IL, USA
 Drug Dev. Res. (1995), 34(3), 267-75
 CODEN: DDREXK; ISSN: 0272-4391
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Treatment with .alpha.1 antagonists represents a pharmacol. alternative to surgery for the treatment of urinary obstruction assocd. with benign prostatic hyperplasia (BPH). A minimally invasive method to measure elevation of prostatic urethral tone through a urethral catheter was used to study the effects of .alpha.-adrenoceptor agonists and antagonists on canine intraurethral pressure (IUP). .alpha.1-Adrenoceptor agonists, but not .alpha.2 agonists, elicited elevations in IUP. The contractile response was primarily the result of prostatic smooth muscle contraction, since it was of smaller magnitude in female dogs or in male dogs outside of the prostatic urethra. The contractile responses to epinephrine obtained in the absence of antagonist on the same or different test dates were highly reproducible in dogs greater than 2 yr of age. The increase in IUP caused by epinephrine was specifically antagonized by alpha.1-adrenoceptor antagonists, in direct proportion to their potency in isolated canine prostatic strips in vitro and in proportion to their affinity at receptors detd. in radioligand binding assays in vitro. These data confirm the role of .alpha.1-adrenoceptors in canine prostatic smooth muscle contraction and this relatively non-invasive in vivo model will allow the study of novel compds. for their effects on canine prostatic tone.
 IT 67339-62-2, AR-C 239
 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (pharmacol. antagonism of .alpha.-adrenergic agonist induced increases in canine intraurethral pressure in vivo)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 136 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

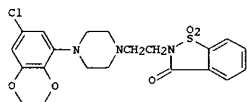


L14 ANSWER 137 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:422806 CAPLUS
 DOCUMENT NUMBER: 122:187611
 TITLE: Preparation of 2,3-dihydro-1,4-benzodioxin-5-yl-piperazine derivatives having 5-HT1A-antagonistic activity.
 INVENTOR(S): Hartog, Jan; Van Steen, B. J.; Mos, Johannes; Schipper, Jacques
 PATENT ASSIGNEE(S): Duphar International Research B.V., Neth.
 SOURCE: Eur. Pat. Appl., 16 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|--|------------|
| EP 633260 | A1 | 19850111 | EP 1994-201900 | 19940701 |
| EP 633260 | B1 | 20011107 | | |
| CA 2127084 | AA | 19950106 | CA 1994-2127084 | 19940629 |
| FI 9403149 | A | 19950106 | FI 1994-3149 | 19940630 |
| NO 9402471 | A | 19950106 | NO 1994-2471 | 19940630 |
| JP 07215972 | A2 | 19950815 | JP 1994-170370 | 19940630 |
| US 5462942 | A | 19951031 | US 1994-269086 | 19940630 |
| HU 75155 | A2 | 19970428 | HU 1994-1965 | 19940630 |
| HU 218215 | B | 20000628 | | |
| CZ 286503 | B6 | 20000412 | CZ 1994-1597 | 19940630 |
| SK 281681 | B6 | 20010611 | SK 1994-788 | 19940630 |
| ZA 9404787 | A | 19950220 | ZA 1994-4787 | 19940701 |
| CN 1106813 | A | 19950816 | CN 1994-115999 | 19940701 |
| CN 1044244 | B | 19990721 | | |
| AT 208385 | E | 20011115 | AT 1994-201900 | 19940701 |
| ES 2167346 | T3 | 20020516 | ES 1994-201900 | 19940701 |
| AU 9466139 | A1 | 19950112 | AU 1994-66139 | 19940704 |
| AU 680900 | B2 | 19970814 | | |
| RU 2118322 | C1 | 19980827 | RU 1994-23250 | 19940704 |
| IL 110209 | A1 | 20000229 | IL 1994-110209 | 19940704 |
| PRIORITY APPLN. INFO.: | | | EP 1993-201950 | A 19930705 |
| OTHER SOURCE(S): | | | CASREACT 122:187611; MARPAT 122:187611 | |
| GI | | | | |



I



II

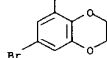
AB Title compds. (I; R1 = halo, lower alkyl, alkoxy, OH, CF3, cyano; m = 1,2; n = 0,1; A = C2-6 alkylene which may be substituted with .gtoreq.1 lower alkyl groups or a monocyclic (hetero)aryl group; B = CH2, CH2CH2, CO, S, SO, SO2), were prepd. Thus, saccharin was heated with 1-(7-chloro-2,3-dihydro-1,4-benzodioxin-5-yl)-4-(2-chloroethyl)piperazine and NaH in DMF to give title compd. (II). In general I were selective for 5-HT1a receptors, antagonize the effects of 8-OH-DPAT in rats, and have good oral bioavailability.

IT 161612-04-0P
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of 2,3-dihydro-1,4-benzodioxin-5-yl-piperazine derivs. having 5-HT1a-antagonistic activity)

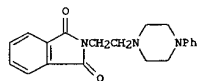
RN 161612-04-0 CAPLUS
 CN 1(2H)-Isoquinolinone, 2-[2-[4-(7-bromo-2,3-dihydro-1,4-benzodioxin-5-yl)-1-piperazinyl]ethyl]-6-chloro-3,4-dihydro-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl



L14 ANSWER 138 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:376590 CAPLUS
 DOCUMENT NUMBER: 122:214029
 TITLE: Structure of N-[2-[4-phenyl-1-piperazinyl]ethyl]phthalimide
 AUTHOR(S): Andronati, S. A.; Simonov, Yu. A.; Dvorkin, A. A.; Bondarev, M. L.; Yavorsky, A. S.; Chumakov, Yu. M.
 CORPORATE SOURCE: Fiz.-Khim. Inst. im. A.V. Bogatskagi, Odessa, Ukraine
 SOURCE: Dopov. Akad. Nauk Ukr. (1993), (11), 136-40
 CODEN: DNUKEM
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 GI

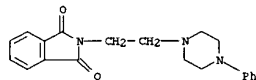


I

AB The structure of the title compd. (I) was detd. by x-ray anal. The distance from the center of the Ph ring to the center of the phthalimide moiety was 9.90 .ANG.. This distance is comparable with that in Humber's model for the dopamine receptor site. Quantum-chem. calcns., along with x-ray data, confirm that the lone electron pair of N-4 of the piperazine fragment is conjugated with the Ph ring.

IT 75000-24-7
 RL: FRP (Properties) (x-ray anal. of)

RN 75000-24-7 CAPLUS
 CN 1H-Iscoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

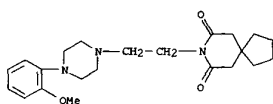


L14 ANSWER 139 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:320486 CAPLUS
 DOCUMENT NUMBER: 122:97160
 TITLE: RMY 7378 is a selective antagonist of the D subtype of .alpha.1-adrenoceptors
 AUTHOR(S): Goetz, Aaron S.; King, Holly K.; Ward, Stuart D. C.; True, Timothy A.; Rimele, Thomas J.; Saussy,, David L.
 CORPORATE SOURCE: Jr. Department of Cellular Biochemistry, Glaxo Research Institute, Five Moore Drive, Research Triangle Park, NC, 27709, USA
 SOURCE: Eur. J. Pharmacol. (1995), 272(2/3), R5-R6
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB RMY 7378 [8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4.5]decane-7,9-dione dihydrochloride), a 5-HT1A receptor partial agonist, also binds to .alpha.1-adrenoceptors. Competition assays were performed using (.+.)-.beta.-([125I]iodo-4-hydroxyphenyl)-ethyl-aminomethyl-tetralone ([125I]HEAT), and membranes prepd. from Rat-1 fibroblasts expressing hamster .alpha.1b-, bovine .alpha.1c-, or rat .alpha.1d-adrenoceptor, or their resp. human homologues. Results indicate that RMY 7378 is selective for the .alpha.1D-adrenoceptor subtype (pKi: hamster .alpha.1b-adrenoceptor 6.2+-0.03, human .alpha.1b-adrenoceptor 7.2+-0.05; bovine .alpha.1c-adrenoceptor 6.1+-0.02, human .alpha.1c-adrenoceptor 6.6+-0.20; rat .alpha.1d-adrenoceptor 8.2+-0.06, human .alpha.1d-adrenoceptor 9.4+-0.05) and has high affinity (pA2, 8.9+-0.1) for rat aorta .alpha.1-adrenoceptor.

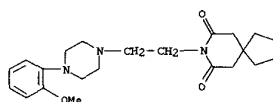
IT 21102-95-4, RMY 7378
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (RMY 7378 is selective antagonist of D subtype of .alpha.1-adrenoceptors)

RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 140 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

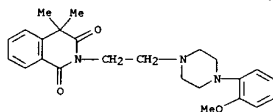


●2 HCl

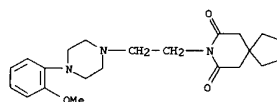
L14 ANSWER 140 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:252067 CAPLUS
 DOCUMENT NUMBER: 122:24395
 TITLE: Differential sensitivity of 3H-agonist binding to pre- and postsynaptic 5-HT1A receptors in bovine brain
 AUTHOR(S): Iben, Lawrence G.; Mahle, Cathy D.; Yocca, Frank D.
 CORPORATE SOURCE: Psychobiol. Disorders, Bristol-Myers Squibb Pharm. Res. Inst., Wallingford, CT, 06492, USA
 SOURCE: Br. J. Pharmacol. (1994), 113(4), 1400-6
 CODEN: BJPCRM; ISSN: 0007-1188
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The full and weak partial 5-HT1A agonist ligands [3H]-8-OH-DPAT and [3H]-RMY-7378 were used to characterize the binding parameters of pre- and postsynaptic 5-HT1A binding sites in bovine dorsal raphe and hippocampal membranes, resp. The Kd and Bmax values for the individual radioligands were indistinguishable across the regions tested, as were the Ki values generated by a series of agents acting at 5-hydroxytryptamine (5-HT) receptors. The concn.-dependent allosteric attenuation of [3H]-8-OH-DPAT and [3H]-RMY-7378 binding produced by the nonhydrolyzable guanyl nucleotide, Gpp(NH)p, generated similar IC50 values within a particular region; however, these were significantly different between regions. While the maximal attenuation of [3H]-8-OH-DPAT and [3H]-RMY-7378 binding was similar in dorsal raphe, Gpp(NH)p produced a significantly greater attenuation of [3H]-8-OH-DPAT binding in hippocampal membranes when compared to [3H]-RMY-7378. The maximal attenuation of [3H]-8-OH-DPAT binding by Gpp(NH)p in hippocampus was also significantly greater than that seen with either radioligand in dorsal raphe. Although exposure to Gpp(NH)p had no effect on the affinity consts. of either radioligand in either region, it produced a concn.-dependent reductn. in the maximal no. of binding sites for both radioligands in both regions. While the percentage reductn. in Bmax values were similar for both radioligands in the dorsal raphe, Gpp(NH)p reduced the Bmax of [3H]-8-OH-DPAT in the hippocampus significantly more than that of [3H]-RMY-7378. These results suggest that while pre- and postsynaptic 5-HT1A receptors may share similar pharmacol. recognition properties, a region-dependent difference in the coupling of the 5-HT1A receptor to G-proteins may exist.
 IT 21102-95-4, RMY-7378
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (serotonin pre- and postsynaptic 5HTA receptor ligand binding similarity)

L14 ANSWER 141 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:247986 CAPLUS
 DOCUMENT NUMBER: 122:24361
 TITLE: Species orthologs of the alpha-2A adrenergic receptor:
 receptor: the pharmacological properties of the bovine and rat
 receptors differ from the human and porcine
 receptors
 AUTHOR(S): O'Rourke, M. F.; Iversen, L. J.; Lomasney, J. W.; Bylund, D. B.
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Nebraska Med. Cent., Omaha, NE, USA
 SOURCE: J. Pharmacol. Exp. Ther. (1994), 271(2), 735-40
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Four pharmacol. subtypes of the alpha-2 adrenergic receptor have been identified; however, only three subtypes exist in any given species. Although the alpha-2A adrenergic receptor, as defined by the human platelet, and the alpha-2D receptor, as defined in the bovine pineal, have very different pharmacol. characteristics, they are more similar to each other than either is to the alpha-2B or alpha-2C subtype. The human alpha-2-C10 clone (alpha-2A) and the rat RG20 clone have an 89% identity in their predicted amino acid sequence and are considered to be species orthologs. Although the expressed RG20 clone appears to have alpha-2D pharmacol., a careful comparison of its pharmacol. characteristics with the bovine pineal has not been reported previously. Based on the pKi values of a panel of 13 alpha-2 adrenergic agents that have been used previously to compare the alpha-2A, alpha-2B and alpha-2C subtypes, the pharmacol. characteristics of the bovine pineal alpha-2D receptor appear to be very similar to the rat RG20 clone (correlation coeff., r, of 0.93). The porcine ortholog of the human alpha-2-C10 receptor has pharmacol. characteristics identical to the human alpha-2A receptor (r = 0.99). Because of its higher affinity for the alpha-2D receptor, [3H]RX 821002 is a better radioligand than [3H]rauwolscine for studying this receptor subtypes.
 IT 67339-62-2, ARC 239
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (pharmacol. of .alpha.2A-adrenergic receptor of bovine and rat differ from human and receptors)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 141 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 142 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:225638 CAPLUS
 DOCUMENT NUMBER: 122:1607
 TITLE: Serotonin inhibition of adenylate cyclase in human platelet membranes; relation to 5-HT-1A receptor-mediated activity
 AUTHOR(S): Newman, Michael E.
 CORPORATE SOURCE: Dep. Psychiat., Hadassah Univ. Hosp., Jerusalem, Israel
 SOURCE: Biochemical Pharmacology (1994), 48(9), 1677-82
 CODEN: BCPCA6; ISSN: 0006-2952
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Serotonin inhibited both basal and forskolin-stimulated adenylate cyclase activity in human platelet membranes by approx. 30%, with an EC50 of 54 nM. Addn. of NaCl to the assay medium reduced the degree of inhibition.
 5-Carboxamidotryptamine (5-CT) behaved as a full agonist in this system (EC50 of 5.4 nM) and BMY 7378 and a partial agonist (inducing 19% inhibition); the putative 5-HT1A receptor agonists metergoline, spiroxatrine and MDL 73005 were inactive. The 5-HT1A receptor antagonists metitepin and NAN-190 behaved as antagonists with Kb or Ki values of 11.2 and 1.17 nM, resp. Spiperone behaved as a partial antagonist only. Epinephrine and 5-HT produced convergent, nonadditive inhibition of both basal and forskolin-stimulated cyclase.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (serotonin inhibition of adenylate cyclase in human platelet membranes in relation to serotoninergic 5IA receptor)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

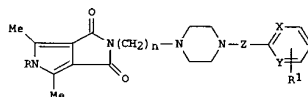


●2 HCl

L14 ANSWER 142 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

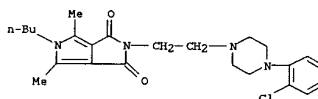
L14 ANSWER 143 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1995:84779 CAPLUS
 DOCUMENT NUMBER: 123:9354
 TITLE: Synthesis and biological evaluation of derivatives of

N-[4-substituted-1-piperazinylalkyl]-1-(butyl,aryl)-2,5-dimethylpyrrole-3,4-dicarboximide (Part II)
 AUTHOR(S): Malinka, Wieslaw; Siskulcka-Dziuba, Maria; Robak, Jacek; Kleinrok, Zdzislaw
 CORPORATE SOURCE: Dep. Drugs Chem., Medical Acad., Wroclaw, 50-137, Pol.
 SOURCE: Farmaco (1994), 49(7-8), 481-7
 CODEN: FRANCES
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



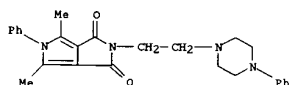
I

AB The title compds. I (n = 2-4; X, Y = CH, N; Z = -, CH2; R = Bu, Ph, 2-MeC6H4; R1 = H, Cl) have been prepd. by reaction of N-haloalkylamide derivs. with the corresponding N-monosubstituted piperazines. I were tested in preliminary pharmacol. investigations, and produced a general depressive action on the central nervous system.
 IT 159658-13-6P 159658-14-7P
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (prepn. and CNS activity of (piperazinylalkyl)pyrroledicarboximides)
 RN 159658-13-6 CAPLUS
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 5-butyl-2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)

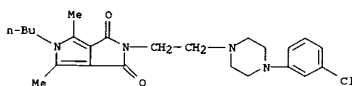


RN 159658-14-7 CAPLUS

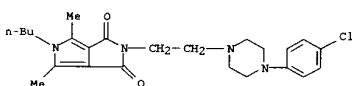
L14 ANSWER 143 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione,
 4,6-dimethyl-5-phenyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



IT 159658-19-2P 159658-20-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and CNS activity of
 (piperazinylalkyl)pyrroledicarboximides)
 RN 159658-19-2 CAPLUS
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione,
 5-butyl-2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)

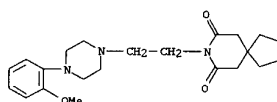


RN 159658-20-5 CAPLUS
 CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione,
 5-butyl-2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-4,6-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 144 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:692532 CAPLUS
 DOCUMENT NUMBER: 121:292532
 TITLE: Effects of the putative 5-hydroxytryptamine1A antagonists BMY 7378, NAN 190 and (-)-propranolol on serotonergic dorsal raphe unit activity in behaving cats
 AUTHOR(S): Fornal, Casimir A.; Marrosu, Franco; Metzler, Christine W.; Tada, Koji; Jacobs, Barry
 CORPORATE SOURCE: Dep. Physiol., Princeton Univ., Princeton, NJ, USA
 SOURCE: J. Pharmacol. Exp. Ther. (1994), 270(3), 1359-66
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Recent evidence from the authors lab. has demonstrated that blockade of somatodendritic 5-hydroxytryptamine (5-HT)1A autoreceptors by systemic administration of spiperone increases the firing rate of central serotonergic neurons in awake cats. The present study exams. the effects of 3 other putative 5-HT1A antagonists (BMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4,5]-decane-7,9-dione), NAN 190 (1-[2-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl]piperazine) and (-)-propranolol) on the single-unit activity of serotonergic neurons recorded in the dorsal raphe nucleus of free-moving cats. Systemic administration of the phenylpiperazine derivs. BMY 7378 (5-100 .mu.g/kg i.v.) and NAN 190 (5-250 .mu.g/kg i.v.) produced a rapid, dose-dependent inhibition of neuronal activity with BMY 7378 being approx. twice as potent as NAN 190 (ED50 = 15.3 .mu.g/kg vs. 34.2 .mu.g/kg). The suppression of neuronal activity produced by both compds. was greatly attenuated by spiperone (1 mg/kg i.v.). Systemic administration of (-)-propranolol (2 and 4 mg/kg i.v.) produced a modest suppression of serotonergic neuronal activity which did not appear to be dose-related. The ability of BMY 7378, NAN 190 and (-)-propranolol to block the suppression of neuronal activity produced by 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT), a selective 5-HT1A agonist, was also examd. Pretreatment with these compds. had no significant effect on the inhibitory response of serotonergic neurons to 8-OH-DPAT challenge. These results indicate that BMY 7378 and NAN 190 act as agonists rather than antagonists at the somatodendritic 5-HT1A autoreceptor. Furthermore, (-)-propranolol, unlike spiperone, does not appear to be an effective 5-HT1A autoreceptor antagonist, because it did not block the action 8-OH-DPAT or increase basal serotonergic neuronal activity in awake animals.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (effects of putative 5-hydroxytryptamine1A antagonists BMY 7378 and NAN

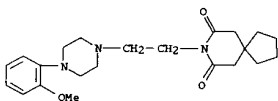
L14 ANSWER 144 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 190 and propranolol on serotonergic dorsal raphe unit activity in behaving cats)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 145 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:596576 CAPLUS
 DOCUMENT NUMBER: 121:196576
 TITLE: Serotonin and pain: Evidence that activation of 5-HT1A receptors does not elicit antinociception against noxious thermal, mechanical and chemical stimuli in mice
 AUTHOR(S): Millan, Mark J.
 CORPORATE SOURCE: Institut de Recherches Servier, Puteaux, 92800, Fr.
 SOURCE: Pain (1994), 58(1), 45-61
 CODEN: PAINDB; ISSN: 0304-3959
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In this study, we examd. whether activation of 5-HT1A receptors elicits antinociception in response to acute noxious chem., thermal and mech. stimuli in mice. In the writhing test, both agonists (e.g., 8-OH-DPAT, S 14671 and WY 50,324) and partial agonists (e.g., buspirone and gepirone) elicited a pronounced antinociception. However, antagonists (e.g., (-)-alprenolol and WAY 100,135) also induced antinociception and, at lower (inactive) doses, failed to modify the action of agonists. In addn., the sepn. between doses required for induction of antinociception as compared to those required for induction of ataxia (in the rotarod test) was variable and low for both agonists (median: 1.9) and partial agonists (median: 1.3), although it was somewhat greater for antagonists (.gtoreq.3.3). In the hot-plate test, only certain agonists (e.g., 8-OH-DPAT) and partial agonists (e.g., gepirone) elicited antinociception and their actions were not attenuated by 5-HT1A antagonists which, themselves, were inactive in this paradigm. The 5-HT1C/2 antagonist, ritanserin, the 5-HT3 antagonist, ondansetron, the dopamine D2 receptor antagonist, raclopride, and the .alpha.1-adrenoceptor antagonist, prazosin, were also ineffective in modifying the antinociception evoked by 5-HT1A agonists and partial agonists in the hot-plate test. In contrast, their actions were strongly attenuated by the .alpha.2-adrenoceptor antagonist, idazoxan. In the tail-flick tests to noxious heat and noxious pressure, 5-HT1A receptor agonists, partial agonists and antagonists generally failed to induce antinociception. Moreover, modulation of stimulus intensity (from very weak to very intense) did not reveal any influence upon the latency to respond. In conclusion, in the writhing test, the data provide no evidence for a specific antinociceptive effect of the activation of 5-HT1A receptors. Further, in the hot-plate test, for those 5-HT1A agonists and partial agonists which induce

L14 ANSWER 145 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 antinociception, .alpha.2-adrenoceptors rather than 5-HT1A receptors
 are implicated in their actions. Finally, in reflexive tests, irresp. of
 stimulus quality or intensity, 5-HT1A agonists and partial agonists
 do not mediate antinociception. These data suggest that the activation of
 5-HT1A receptors does not, under these conditions of acute noxious
 stimulation, elicit antinociception.
 IT 21102-95-4, BMY 7378
 RL: BAC (Biological activity or effector, except adverse); THU
 (Therapeutic use); BIOL (Biological study); USES (Uses)
 (antinociception against noxious thermal, mech. and chem. stimuli
 in mice)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L14 ANSWER 146 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:509676 CAPLUS
 DOCUMENT NUMBER: 121:109676
 TITLE: Preparation of N-(2-oxoethyl)amino acid
 derivatives
 INVENTOR(S): and peptides as immunosuppressants
 Michael, Connell, Richard D.; Osterman, David D.; Katz,
 E.
 PATENT ASSIGNEE(S): Miles Inc., USA
 SOURCE: Eur. Pat. Appl., 96 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| EP 564924 | A2 | 19931013 | EP 1993-105035 | 19930326 |
| EP 564924 | A3 | 19931229 | | |
| EP 564924 | B1 | 19980909 | | |

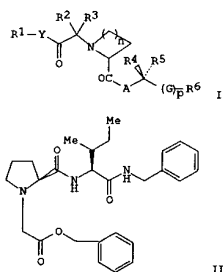
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL,
 PT, SE

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|-------------|----|----------|-----------------|----------|
| CA 2091194 | AA | 19931009 | CA 1993-2091194 | 19930308 |
| AT 170870 | E | 19980915 | AT 1993-105035 | 19930326 |
| ES 2119826 | T3 | 19981016 | ES 1993-105035 | 19930326 |
| AU 9336773 | A1 | 19931014 | AU 1993-36773 | 19930406 |
| AU 666179 | B2 | 19960201 | | |
| JP 06041064 | A2 | 19940215 | JP 1993-106160 | 19930408 |
| US 5686424 | A | 19971111 | US 1995-431390 | 19950428 |

PRIORITY APPLN. INFO.: US 1992-864998 19920408
 US 1992-981565 19921125

OTHER SOURCE(S): MARPAT 121:109676
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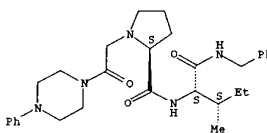
L14 ANSWER 146 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB Title compds. I [R1 = H, (un)substituted alkyl, (un)substituted
 alkenyl,
 cycloalkyl, etc.; Y = bond, O, (un)substituted imino; R1-Y =
 (un)substituted heterocyclyl; one of R2 and R3 = H and the other =
 alkyl;
 n = 2, 3; A = O, (un)substituted imino; R4, R5 = H, (un)substituted
 alkyl,
 etc.; G = CH=CH, CH2-CH2, CH2, NHCO; R6 = H, (un)substituted alkyl,
 (un)substituted Ph, etc.; p = 0, 1] are prepd. E.g., L-proline-L-
 isoleucine benzylamide (prepn. given) in MeCN was refluxed with
 benzyl
 2-bromoacetate to give the title compd. II. In an in vitro study,
 this
 had an IC50 of 2.2 .mu.M against peptidyl prolyl isomerase.
 IT 156800-43-0P
 RL: BAC (Biological activity or effector, except adverse); SPN
 (Synthetic
 Preparation); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (prepn. of, as immunosuppressant)
 RN 156800-43-0 CAPLUS
 CN L-isoleucinamide,
 1-[2-oxo-2-(4-phenyl-1-piperazinyl)ethyl]-L-prolyl-N-
 (phenylmethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

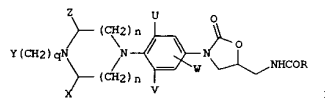
L14 ANSWER 146 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:323599 CAPLUS
DOCUMENT NUMBER: 120:323599
TITLE: Oxazolidinones antibiotics containing a substituted
inventor(s): diazine moiety
Hutchinson, Douglas K.; Brickner, Steven Joseph;
Barbachyn, Michael Robert; Gammill, Ronald B.;
Patel, Maheest V.
PATEM ASSIGNEE(S): Upjohn Co., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATEM INFORMATION:

| PATEM NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|--|-----------------|-------------|
| WO 9323384 | A1 | 19931125 | WO 1993-US3570 | 19930421 |
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| RW: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, EF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| AU 9342877 | A1 | 19931213 | AU 1993-42877 | 19930421 |
| AU 668733 | B2 | 19960516 | | |
| EP 640077 | A1 | 19950301 | EP 1993-912267 | 19930421 |
| EP 640077 | B1 | 20020626 | | |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT | | | |
| JP 07506829 | T2 | 19950727 | JP 1993-520226 | 19930421 |
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| HU 72296 | A2 | 19960429 | HU 1994-3208 | 19930421 |
| CZ 281884 | B6 | 19970312 | CZ 1994-2505 | 19930421 |
| RU 2105003 | C1 | 19980220 | RU 1994-46011 | 19930421 |
| PL 174850 | B1 | 19980530 | PL 1993-321588 | 19930421 |
| PL 174909 | B1 | 19981030 | PL 1993-306030 | 19930421 |
| AT 219770 | E | 20020715 | AT 1993-912267 | 19930421 |
| ZA 9302855 | A | 19941024 | ZA 1993-2855 | 19930422 |
| IL 105555 | A1 | 19980715 | IL 1993-105555 | 19930429 |
| CN 1079964 | A | 19931229 | CN 1993-105039 | 19930508 |
| CN 1044236 | B | 19990721 | | |
| NO 9404237 | A | 19950104 | NO 1994-4237 | 19941107 |
| FI 9405246 | A | 19941108 | FI 1994-5246 | 19941108 |
| PRIORITY APPLN. INFO.: | | | US 1992-880432 | A1 19920508 |
| | | | WO 1993-US3570 | A 19930421 |
| OTHER SOURCE(S): | MARPAT 120:323599 | | | |
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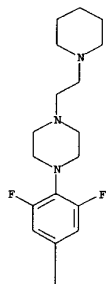
L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



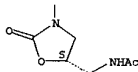
AB The title compds. [1; R = H, (un)substituted C1-6 alkyl, C3-12 cycloalkyl, C1-6 alkoxy, etc.; U, V, W = (un)substituted C1-6 alkyl, F, Cl, Br, H; X, Z = C1-6 alkyl, C3-12 cycloalkyl, H; Y = H, C1-6 alkyl, aryl, OH, (un)substituted PhO, (un)substituted piperidino, etc.], effective against members of human and veterinary pathogens, including multiple-drug-resistant Staphylococci, Streptococci, anaerobic organisms such as Bacteroides and Clostridia, and acid-fast organisms such as Mycobacterium tuberculosis and Mycobacterium avium, are prepd. Thus, Me 4-[4-[5-[(acetylamino)methyl]-2-oxo-3-oxazolidinyl]-2-fluorophenyl]-1-piperazinecarboxylate, prepd. from 3,4-difluoronitrobenzene in 12 steps, demonstrated 50% oral ED in the Murine Assay procedure using female mice injected with S. aureus (UC# 6685) of 4.0 mg/kg, vs. 6.6 for ciprofloxacin.
IT 154590-81-5 154590-90-6
RL: RCT (Reactant)
(prepn. as antibiotic)
RW 154590-81-5 CAPLUS
CN Acetamide, N-[[3-[3,5-difluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-, (S)- (9CI) (CA INDEX NAME)
Absolute stereochemistry.

L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

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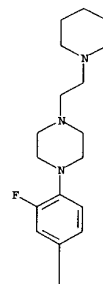
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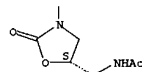
RN 154590-90-6 CAPLUS
CN Acetamide, N-[[3-[3-fluoro-4-[4-[2-(1-piperidinyl)ethyl]-1-piperazinyl]phenyl]-2-oxo-5-oxazolidinyl]methyl]-, (S)- (9CI) (CA INDEX NAME)
Absolute stereochemistry.

L14 ANSWER 147 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PAGE 1-A

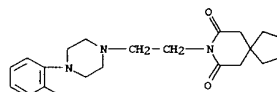


PAGE 2-A



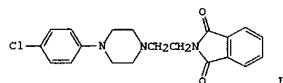
L14 ANSWER 148 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:316528 CAPLUS
 DOCUMENT NUMBER: 120:316528
 TITLE: Differential effects of N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ) on various 5-HT receptor binding sites in the rat brain
 AUTHOR(S): Gozlan, H.; Laporte, A. M.; Thibault, S.;
 Schechter, L. E.; Bolanos, F.; Hamon, M.
 CORPORATE SOURCE: INSERM U 288/Neurobiol. Cell. Fonctionnelle, Fac. Med.
 SOURCE: Pitie-Salpetriere, Paris, 75634, Fr. Neuropharmacology (1994), 33(3-4), 423-31
 CODEN: NEPHEW; ISSN: 0028-3908
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The effects of N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ), an alkylating agent producing irreversible blockade of various membrane bound receptors in brain, were investigated on four different types of serotonin receptors, 5-HT1A, 5-HT1B, 5-HT2A and 5-HT3, in various brain regions in the rat. In addn., the fate of central benzodiazepine- and R-zacopride-specific binding sites was also examd. in rats treated with EEDQ. Membrane binding assays and/or quant. autoradiog. with appropriate radioligands indicated that EEDQ inactivated 5-HT1A, 5-HT1B and 5-HT2A sites, but was poorly active on 5-HT3, benzodiazepine and "R" sites. Among the receptors affected by EEDQ, hippocampal 5-HT1A sites were the most sensitive to the alkylating agent (ID50.apprx.1 mg/kg i.p.), followed by the cortical 5-HT2A (ID50.apprx.6 mg/kg i.p.) sites. Pretreatment by selective ligands partially protected hippocampal 5-HT1A sites from irreversible inactivation by EEDQ (10 mg/kg i.p.) with the following order of efficacy: WAY 100135 > spiperone > BMY 7378 > ipsapirone. Similarly, pretreatment by spiperone (5 mg/kg i.p.) also reduced the ability of EEDQ to inactivate cortical 5-HT2A receptors. Analyses of the time-course recovery of resp. binding sites after EEDQ administration showed that the turnover rate of 5-HT1A sites did not significantly differ in the dorsal raphe nucleus and in various forebrain areas (hippocampus, septum, cerebral cortex; half-life .apprx.4 days), but was lower than that of cortical 5-HT2A sites (half-life: 2.9 days).
 IT 21102-95-4, BMY 7378
 RL: BIOL (Biological study)
 (serotonin receptor binding by, receptor inactivation by EEDQ)

L14 ANSWER 148 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 prevention by, in brain)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



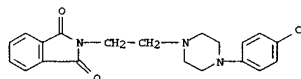
● 2 HCl

L14 ANSWER 149 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:261043 CAPLUS
 DOCUMENT NUMBER: 120:261043
 TITLE: Long lasting inhibition of food intake in the rat by a new phthalimidoethylpiperazine derivative
 AUTHOR(S): Mustafa, A. A.; Al-Rashood, K. A.; El-Obeid, H.
 A. Arabia
 CORPORATE SOURCE: Coll. Med., King Saud Univ., Riyadh, 11461, Saudi Arabia
 SOURCE: Res. Commun. Psychol., Psychiatry Behav. (1993), 18(1-2), 25-36
 CODEN: RCPBDC; ISSN: 0362-2428
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI

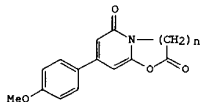
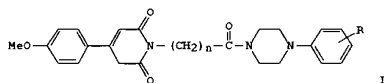


AB 1-[(P-Chlorophenyl)-4-(phthalimidoethyl)]piperazine (I; CPPEP), a newly synthesized compd., produced a dose-dependent inhibition of food intake in food-deprived male Wistar rats. This effect was still apparent three days after injection of the compd. The anorectic effect was not antagonized by either the non-selective 5-HT receptor antagonist, methylsergide (5 mg kg-1, i.p.), nor by the 5-HT2 receptor antagonist, ketanserin (1 mg kg-1, i.p.), pindolol (4 mg kg-1, i.p.), which blocks .beta.-adrenoceptors and some of the effects mediated at 5-HT1 receptors, did not block the redn. in food intake produced by the compd. Similarly the non-selective alpha-adrenoceptor antagonist, phentolamine (5 mg kg-1, i.p.) and the .alpha.2-adrenoceptor blocker, yohimbine (2 mg kg-1, i.p.) did not affect the anorectic effect of CPPEP. The hypophagic effect of CPPEP, however, was antagonized by the D2-dopamine receptor blocker, (.+-.) sulpiride (30 mg kg-1, i.p.) and by the relatively selective 5-HT3 receptor antagonist, zacopride (1 mg kg-1, i.p.). None of the antagonists used had any effect on food intake when they were administered alone. It is concluded that

L14 ANSWER 149 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 the anorectic action of CPPEP is mediated, at least in part, by interaction with 5-HT3 receptors.
 IT 75000-30-5
 RI: PRP (Properties)
 (long-lasting anorectic effect of, serotoninergic S3 receptors in)
 RN 75000-30-5 CAPLUS
 CN 1H-Indole-1,3(2H)-dione, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

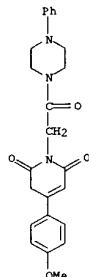


L14 ANSWER 150 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:244969 CAPLUS
 DOCUMENT NUMBER: 120:244969
 TITLE: Synthesis of 1-arylpiperazine amides of 2-[4-(methoxyphenyl)-1H,5H-pyridin-2,6-dione-1-yl]acetic, -propionic acids
 AUTHOR(S): Thakur, K. D.; Samant, S. D.
 CORPORATE SOURCE: Org. Chem. Res. Lab., Univ. Dep. Chem. Technol., Bombay, 400 019, India
 SOURCE: J. Indian Chem. Soc. (1993), 70(3), 261-3
 CODEN: JICSAH; ISSN: 0019-4522
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 120:244969
 GI

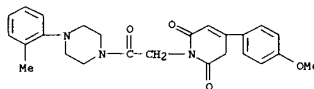


AB The title compds. I (R = H, 2-, 3-, 4-Me, 3-, 4-Cl, n = 1, 2) were
 prepd. by condensing oxazolo[oxazinopyridinediones II with the corresponding
 arylpiperazine.
 IT 154147-05-4P 154147-06-5P 154147-07-6P
 154147-08-7P 154147-09-8P 154147-10-1P
 RL: SPN (Synthetic preparation); PREF (Preparation)
 (prepn. of)
 RN 154147-05-4 CAPLUS
 CN Piperazine, 1-[[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-dioxo-1(2H)-
 pyridinyl]acetyl]-4-phenyl- (9CI) (CA INDEX NAME)

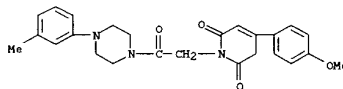
L14 ANSWER 150 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 154147-06-5 CAPLUS
 CN Piperazine, 1-[[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-dioxo-1(2H)-
 pyridinyl]acetyl]-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)

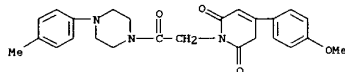


RN 154147-07-6 CAPLUS
 CN Piperazine, 1-[[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-dioxo-1(2H)-
 pyridinyl]acetyl]-4-(3-methylphenyl)- (9CI) (CA INDEX NAME)

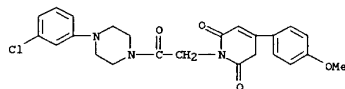


RN 154147-08-7 CAPLUS
 CN Piperazine, 1-[[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-dioxo-1(2H)-
 pyridinyl]acetyl]-4-(4-methylphenyl)- (9CI) (CA INDEX NAME)

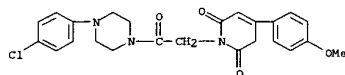
L14 ANSWER 150 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



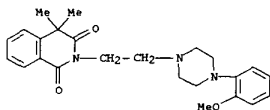
RN 154147-09-8 CAPLUS
 CN Piperazine, 1-[[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-
 dioxo-1(2H)-pyridinyl]acetyl]-4-(3-chlorophenyl)- (9CI) (CA INDEX NAME)



RN 154147-10-1 CAPLUS
 CN Piperazine, 1-[[[3,6-dihydro-4-(4-methoxyphenyl)-2,6-
 dioxo-1(2H)-pyridinyl]acetyl]-4-(4-chlorophenyl)- (9CI) (CA INDEX NAME)

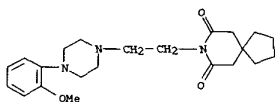


L14 ANSWER 151 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:182875 CAPLUS
 DOCUMENT NUMBER: 120:182875
 TITLE: Further characterization of human .alpha.2-adrenoceptor subtypes: [3H]RX821002 binding and definition of additional selective drugs
 AUTHOR(S): Devedjian, Jean Christophe; Esclapez, Francoise; Denis-Pouxviel, Colette; Paris, Herve
 CORPORATE SOURCE: Inst. Louis Bugnard, CHU Rangueil, Toulouse, 31054, Fr.
 SOURCE: Eur. J. Pharmacol. (1994), 252(1), 43-9
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The characteristics of [3H]RX821002 binding to the different human
 .alpha.2-adrenoceptor subtypes were studied on membranes from COS-7
 cells transfected with the genes: .alpha.2C2, .alpha.2C4 and .alpha.2C10.
 Satn. expts. indicated that the radioligand labels the three adrenoceptors
 with high affinity. A difference was however obsd. between the subtypes.
 The affinity of [3H]RX821002 for .alpha.2C10-adrenoceptors (KD = 1.41 +/-
 0.15 nM) was 3-fold higher than for .alpha.2C4-adrenoceptors (KD =
 4.42 +/- 0.63 nM) and 7-fold higher than for .alpha.2C2-adrenoceptors (KD
 = 10.2 +/- 0.9 nM). Inhibition expts. with a series of 17 competitors
 confirmed that prazosin, oxymetazoline, WB4101, ARC239, corynanthine
 and chlorpromazine are subtype-selective drugs. They also demonstrated
 that BRL44408 and guanfacine are selective for the .alpha.2C10-receptor,
 whereas BRL41932 and imiloxan are selective for the .alpha.2C2. Given
 that these two latter drugs were previously shown to be specific for
 the .alpha.2B pharmacol. subtype originally defined in neonatal rat lung,
 these results confirm that the .alpha.2C2 gene encodes for the human
 homolog of this receptor subtype. It is concluded that the combined
 use of [3H]RX821002 and of these new selective drugs may be useful for the
 identification of the .alpha.2-adrenoceptor subtypes in human tissues.
 IT 67339-62-2, ARC239
 RL: BIOL (Biological study)
 (.alpha.2-adrenoceptor subtypes binding of, in human cell
 membranes)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-(4-(2-methoxyphenyl)-1-
 piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 152 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:96856 CAPLUS
 DOCUMENT NUMBER: 120:96856
 TITLE: Electrophysiological evidence for a large receptor reserve for inhibition of dorsal raphe neuronal firing
 firing by 5-HT1A agonists
 AUTHOR(S): Cox, Richard F.; Meller, Emanuel; Waszczak, Barbara L.
 CORPORATE SOURCE: Bouve Coll. Pharm. Health Sci., Northeast. Univ., Boston, MA, 02115, USA
 SOURCE: Synapse (N. Y.) (1993), 14(4), 297-304
 CODEN: SYNAET; ISSN: 0887-4476
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Previous studies (Meller et al. 1990) have shown that a large receptor reserve exists for the inhibition of 5-HT synthesis in rat cortex and hippocampus by the 5-HT1A agonist 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT), whereas little or no reserve exists for the lower efficacy agonists ipsapirone and RMY 7378. The current studies were undertaken to det. if the above drugs exhibit similar relative efficacies and reserves in an electrophysiol. model of 5-HT1A receptor activation, i.e., the inhibition of dorsal raphe cell firing. 1.v. dose-response curves were constructed in untreated control rats, or in rats which received an injection of the irreversible receptor inactivator N-ethoxycarbonyl-2-ethoxy-1,2-dihydroquinoline (EEDQ, 6 mg/kg, s.c.) 24 h before recording. All 3 drugs fully inhibited dorsal raphe cell firing in control rats (ED50's: 1.5 .mu.g/kg, 8-OH-DPAT; 30.0 .mu.g/kg, ipsapirone; 17.5 .mu.g/kg, RMY 7378). However, unlike effects on 5-HT synthesis, EEDQ treatments caused no depression of the maximal inhibitory response for any of the agonists, although all dose-response curves were shifted to the right (ED50's: 10.1 .mu.g/kg, 6.7-fold shift, 8-OH-DPAT; 139.9 .mu.g/kg, 4.7-fold shift, ipsapirone; 53.8 .mu.g/kg, 3.1-fold shift, RMY 7378). Although the order of agonist efficacies was similar for both inhibition of 5-HT synthesis and dorsal raphe cell firing (8-OH-DPAT > ipsapirone > RMY 7378), a large (>50%) receptor reserve was estd. for all 3 drugs in this electrophysiol. system. This suggests that 5-HT1A receptor populations mediating the inhibition of transmitter synthesis and neuronal firing may be differently regulated or have different receptor-effector coupling characteristics (G-proteins, effectors, and/or transduction efficiencies).
 IT 21102-95-4, RMY 7378
 RL: BIOL (Biological study)

L14 ANSWER 152 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 (dorsal raphe neuron firing inhibition by, receptor reserve for serotonin formation inhibition and)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

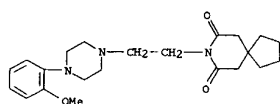


●2 HCl

L14 ANSWER 153 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:95766 CAPLUS
 DOCUMENT NUMBER: 120:95766
 TITLE: Preparation containing interferon-.alpha. and histamine, serotonin or substances with corresponding receptor activity for activation of natural killer cells
 INVENTOR(S): Hellstrand, Kristoffer; Hermansson, Svante
 PATENT ASSIGNEE(S): Estero-Anstalt, Liechtenstein
 SOURCE: PCT Int. Appl., 24 pp.
 CODEN: PIXX02
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|--|----------|-----------------|------------|
| WO 9324144 | A1 | 19931209 | WO 1993-SE496 | 19930603 |
| W: | AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KR, KZ, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US, VN | | | |
| RW: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, RF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| SE 9201719 | A | 19931204 | SE 1992-1719 | 19920603 |
| SE 513429 | C2 | 20000911 | | |
| AU 9343660 | A1 | 19931230 | AU 1993-43660 | 19930603 |
| AU 672610 | B2 | 19961010 | | |
| EP 652768 | A1 | 19950517 | EP 1993-913731 | 19930603 |
| EP 652768 | B1 | 20000503 | | |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | |
| JP 08502024 | T2 | 19960305 | JP 1993-500471 | 19930603 |
| JP 2886259 | B2 | 19990510 | | |
| ES 2147758 | T3 | 20001001 | ES 1993-913731 | 19930603 |
| US 5728378 | A | 19980317 | US 1995-374787 | 19950508 |
| PRIORITY APPLN. INFO.: | | | SE 1992-1719 | A 19920603 |
| | | | WO 1993-SE496 | A 19930603 |
| AB Pharmaceutical prepn. for activation of natural killer cells, for example in order to treat tumors or virus infections, comprises a first compn. contg. interferon-.alpha. or analogs thereof, together with a second compn. contg. at least one substance with H2 or 5-HT1A receptor agonist activity, for example, histamine or serotonin. The first and second compns. are either mixed in a prepn. or furnished in sep. doses. A combination of interferon-.alpha. and histamine showed a synergistic antitumor activity of natural killer cells against cultured target cells. IT 21102-95-4, RMY 7378 RL: BIOL (Biological study) (natural killer cell activation by .alpha.-interferon and) RN 21102-95-4 CAPLUS | | | | |

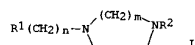
L14 ANSWER 153 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

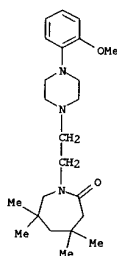
L14 ANSWER 154 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1994:77181 CAPLUS
 DOCUMENT NUMBER: 120:77181
 TITLE: Preparation of hexahydroazepine derivatives as 5-HT1A serotonergic receptor antagonists
 INVENTOR(S): Takahashi, Nobuyuki; Suzuki, Yukio; Mochizuki, Daisuke; Tsujita, Ryuichi; Yaso, Masao; Komaki, Hisayuki
 PATENT ASSIGNEE(S): Asahi Kasei Kogyo K. K., Japan
 SOURCE: PCT Int. Appl., 145 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|--------------------------------------|----------|
| WO 9311116 | A1 | 19930610 | WO 1992-JP1533 | 19921124 |
| W: CA, US | | | | |
| FW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| JP 05345764 | A2 | 19931227 | JP 1992-307377 | 19921117 |
| PRIORITY APPLN. INFO.: | | | JP 1991-336053 | 19911126 |
| | | | JP 1992-307377 | 19921117 |
| OTHER SOURCE(S): | | | CASREACT 120:77181; MARPAT 120:77181 | |
| G1 | | | | |

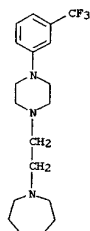


AB The title compds. [I; R1 = (un)substituted hexahydroazepin-1-yl; R2 = (un)substituted Ph, e.g., (trifluoromethyl)phenyl, (un)substituted pyridazinyl or 1,2-benzisothiazolyl; n = 2-5 integer; m = 2, 3],
 5-HT1A serotonergic receptors and therefore useful for treatment of many ailments, e.g., anxiety, depression, motion sickness, hypertension (no data), are prepd. E.g., caprolactam was treated with Cl-(CH2)3-Br in THF contg. NaH at room temp. for 5 h to give 1-(3-chloropropyl)hexahydro-1H-azepine, which was refluxed with 1-[3-(trifluoromethyl)phenyl]piperazine in benzene contg. Et3N for 139 h to give I [R1 = hexahydro-1H-azepin-1-yl, R2 = 3-(trifluoromethyl)phenyl, n = 3, m = 2], which had an affinity (Ki) of 13.7 nM for 5-HT1A receptors.
 IT 151142-17-5P 151142-46-0P 151142-47-1P 151142-48-2P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of, as serotonergic receptor antagonist)
 RN 151142-17-5 CAPLUS

L14 ANSWER 154 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN 2H-Azepin-2-one, hexahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4,6,6-tetramethyl- (9CI) (CA INDEX NAME)

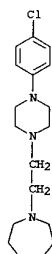


RN 151142-46-0 CAPLUS
 CN 1H-Azepine, hexahydro-1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

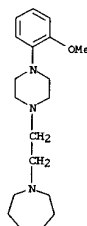


RN 151142-47-1 CAPLUS
 CN 1H-Azepine, 1-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]hexahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 154 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

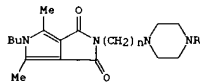


RN 151142-48-2 CAPLUS
 CN 1H-Azepine, hexahydro-1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 155 OF 263 CAPLUS COPYRIGHT 2002 ACS

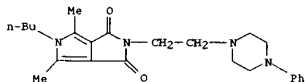
ACCESSION NUMBER: 1994:45179 CAPLUS
DOCUMENT NUMBER: 120:45179
TITLE: Synthesis and pharmacological properties of N-(4-substituted-1-piperazinylalkyl)-1-butyl-2,5-dimethylpyrrole-3,3-dicarboxyimide derivatives
AUTHOR(S): Malinka, Wieslaw; Tatarczyńska, Ewa
CORPORATE SOURCE: Dep. Pharm., Med. Acad. Wrocław, Wrocław,
51-137, Pol.
SOURCE: Farmaco (1993), 48 (7), 933-47
CODEN: FMCE8
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



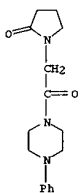
AB The prepn. of a no. of title compds. (I; R = ph, Me, pyridinyl, pyrimidinyl) is described. The structures of the novel compds. were confirmed by elemental and spectral analyses. The results of a preliminary pharmacol. study of CNS effects caused by I are presented.

IT 151722-70-2#
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (prepn. and pharmacol. of, structure in relation to)

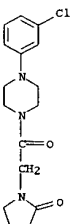
RN 151722-70-2 CAPLUS
CN Pyrrolo[3,4-c]pyrrole-1,3(2H,5H)-dione, 5-butyl-4,6-dimethyl-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 156 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)



RN 131028-02-9 CAPLUS
CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI) (CA INDEX NAME)

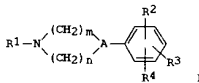


RN 135459-98-2 CAPLUS
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 156 OF 263 CAPLUS COPYRIGHT 2002 ACS

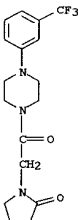
ACCESSION NUMBER: 1994:8615 CAPLUS
DOCUMENT NUMBER: 120:8615
TITLE: Phenyl-substituted heterocyclic antiviral agents
INVENTOR(S): Kuroono, Masayasu; Baba, Yutaka; Iwata, Noriyuki; Kakigami, Takuji; Isogawa, Kogaku; Mitani, Takahiko;
Takahiko; Ishiwata, Yoshiro; Yokochi, Shoji; Otsuka, Tamaki; et al.
PATENT ASSIGNER(S): Sanwa Kagaku Kenkyusho Co., Ltd., Japan
SOURCE: Eur. Pat. Appl., 35 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| EP 548798 | A1 | 19930630 | EP 1992-121466 | 19921217 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 05255089 | A2 | 19931005 | JP 1992-343127 | 19921130 |
| PRIORITY APPLN. INFO.: | | | JP 1991-335028 | 19911218 |
| OTHER SOURCE(S): | | | MARPAT 120:8615 | |
| GI | | | | |

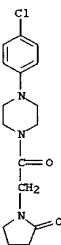


AB The title compds. I [A = N, CH2; R1 = alkyl, acyl, arylsulfonyl, alkylsulfonyl, Ph, heterocyclic; R2-R4 = H, NH2, alkylamino, acylamino, alkyl, HO, alkyloxy, halogen, CO2H, NO2, cyano, SH, etc.; m = 0, natural no.; n = natural no.], useful against infectious diseases caused by DNA viruses, RNA viruses, or retroviruses, are prepd. Thus, 1-(2-chlorophenyl)piperazine was condensed with Me 2-pyrrolidone-1-acetate, producing 1-(2-chlorophenyl)-4-(2-pyrrolidone-1-ylacetyl)piperazine (II) in 77.1% yield. II demonstrated no tissue cytotoxicity and had antiviral activity against herpes simplex virus type 1 at 10 .mu.g/mL.
IT 131027-95-7 131028-02-9 135459-98-2 150558-40-0 150558-41-1 150558-42-2
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study) (antiviral activity of)
RN 131027-95-7 CAPLUS

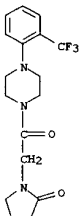
L14 ANSWER 156 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



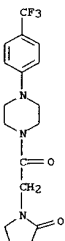
RN 150558-40-0 CAPLUS
CN Piperazine, 1-(4-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI) (CA INDEX NAME)



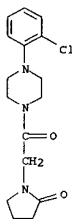
RN 150558-41-1 CAPLUS
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[2-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)



RN 150558-42-2 CAPLUS
 CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[(trifluoromethyl)phenyl]-
 (9CI) (CA INDEX NAME)

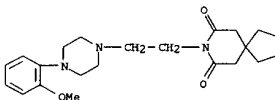


IT 150557-71-4P
 RL: BAC (Biological activity or effector, except adverse); SPN
 (Synthetic
 preparation); BIOL (Biological study); PREP (Preparation)
 (prepn. and antiviral activity of)
 RN 150557-71-4 CAPLUS
 CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[(2-chlorophenyl)phenyl]-
 (9CI)
 (CA INDEX NAME)



L14 ANSWER 157 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1993:531752 CAPLUS
 DOCUMENT NUMBER: 119:131752
 TITLE: Identification of residues important for ligand binding to the human 5-hydroxytryptamine1A serotonin receptor
 AUTHOR(S): Chanda, Pranab K.; Minchin, Michael C. W.; Davis, Alan
 R.; Greenberg, Lynda; Reilly, Yvonne; McGregor, William H.; Bhat, Ramesh; Lubeck, Michael B.; Hung,
 Paul P.
 CORPORATE SOURCE: Dep. Biotechnol. Microbiol., Wyeth-Ayerst Res., Philadelphia, PA, 19101, USA
 SOURCE: Mol. Pharmacol. (1993), 43(4), 516-20
 CODEN: MOPMA3; ISSN: 0026-895X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The functional significance of the conserved amino acids within transmembrane regions II and VII of the human 5-hydroxytryptamine (5-HT)1A receptor was analyzed by oligonucleotide-directed mutagenesis followed by transient expression of the mutated receptor genes in COS-1 cells. The substitution of a conserved asparagine at position 396 (transmembrane region VII) with either alanine, phenylalanine, or valine resulted in a receptor that did not bind the 5-HT1A agonist 8-hydroxy-2-(di-n-[3H]propylamino)tetralin. In contrast, replacement of Asn396 with glutamine did not affect agonist binding. In addn., serine residues at positions 391 and 393 (transmembrane domain VII) were changed to alanine. Changing the less conserved Ser391 to alanine had no effect on ligand binding. However, replacement of the conserved Ser393 with alanine reduced ligand binding by 86%. Replacement of a conserved aspartate at position 82 (transmembrane region II) with alanine also produced a receptor without detectable agonist binding. Protein immunoblotting detected receptor protein of approx. 51 kDa in both wild-type and mutant receptor-expressing cells, indicating that these mutations probably did not affect expression or processing of the protein. Importantly, the sequence of the human 5-HT1A receptor described in this paper differs from the published sequence in transmembrane region IV. The present sequence encodes a protein of 422 amino acids, instead of the 421-amino acid protein that has been described previously and has a change in the sequence in transmembrane region IV from...RPRAL... to...RRAAA..., which corresponds to the published sequence of the rat 5-HT1A receptor. Moreover, conversion of the transmembrane region IV sequence of the present clone to that of the published sequence by site-directed

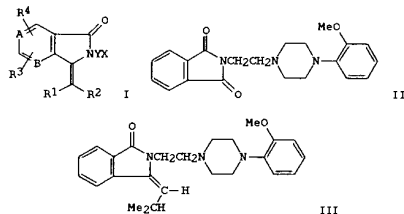
L14 ANSWER 157 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 mutagenesis abolished ligand binding to the receptor.
 IT 21102-95-4
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); PRP (Properties); BIOL (Biological study)
 (5-HT1A receptor of human binding by, site for)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

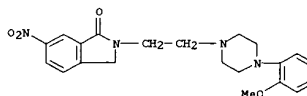
L14 ANSWER 158 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1993:495325 CAPLUS
 DOCUMENT NUMBER: 119:95325
 TITLE: Preparation of 3-methyleneisindolin-1-one derivatives
 INVENTOR(S): Mohri, Shinichiro; Obase, Hiroyuki; Ikeda, Junichi;
 KUBO, Kazuhiro; MORI, Akihisa; ISHII, AKIO
 KYOWA HAKKO KOGYO CO., LTD., JAPAN
 PCT Int. Appl., 185 pp.
 CODEN: F1XX02
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9217448 | A1 | 19921015 | WO 1992-JP246 | 19920302 |
| W: CA, JP, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| PRIORITY APPLN. INFO.: JP 1991-68379 19910401 | | | | |
| OTHER SOURCE(S): MARPAT 119:95325 | | | | |

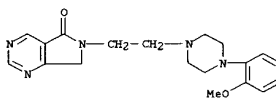


AB The title compds. [I; A, B = CH, N; R1, R2 = alkyl; R3, R4 = halo, alkoxy, etc.; X = (substituted) heterocyclyl; Y = (CH2)1-4] are prepd. A soln. of Me2CHCH2MgBr in THF was added to a soln. of imide II in THF with stirring at room temp. under Ar, 4 N HCl was added with stirring, followed by H2O and 10 N NaOH, and the mixt. was extd. with EtOAc to give 50% III, which as a phosphate salt showed min. ED of 6.3 mg/kg p.o. for cerebral

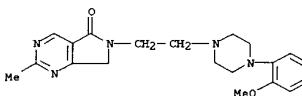
L14 ANSWER 158 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 protection in mice.
 IT 149263-56-9P 149263-60-5P 149263-65-0P
 149263-66-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and reaction of, in prepn. of ischemic cerebral disease drug)
 RN 149263-56-9 CAPLUS
 CN 1H-Isindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-6-nitro- (9CI) (CA INDEX NAME)



RN 149263-60-5 CAPLUS
 CN 5H-Pyrrolo[3,4-d]pyrimidin-5-one, 6,7-dihydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

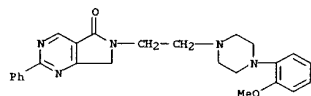


RN 149263-65-0 CAPLUS
 CN 5H-Pyrrolo[3,4-d]pyrimidin-5-one, 6,7-dihydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-2-methyl- (9CI) (CA INDEX NAME)



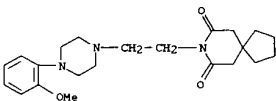
RN 149263-66-1 CAPLUS
 CN 5H-Pyrrolo[3,4-d]pyrimidin-5-one, 6,7-dihydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-2-phenyl- (9CI) (CA INDEX NAME)

L14 ANSWER 158 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 159 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1993:421024 CAPLUS
 DOCUMENT NUMBER: 119:21024
 TITLE: Studies of the biochemical basis for the discriminative properties of 8-hydroxy-2-(di-n-propylamino)tetralin
 AUTHOR(S): Rabin, Richard A.; Winter, J. C.
 CORPORATE SOURCE: Dep. Pharmacol., State Univ. New York, Buffalo, NY, 14214, USA
 SOURCE: Eur. J. Pharmacol. (1993), 235 (2-3), 237-43
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The ability of a series of compds. to mimic the stimulus properties of 8-hydroxy-2-(di-n-propylamino)tetralin (8-OH-DPAT) was compared to: the affinity of these compds. for the 5-HT1A receptor; and their efficacy to inhibit forskolin-stimulated adenylate cyclase activity. Although for 9 compds. (flexinokan, MDL 73005EF, gepirone, ipsapirone, buspirone, tandospirone, yohimbine, L 657,743 and rauwolfscine) complete cross generalization was assocd. with high affinity for the 5-HT1A receptor, eltoprazine, LSD and RMY 7378 had pKD > 7.44, but did not show complete mimicry of 8-OH-DPAT. In addn., indorenate had a pKD of 7.88, yet the behavioral response was indistinguishable from the saline control. Because the above data indicated that affinity for the 5-HT1A receptor was necessary, but not sufficient for a receptor ligand to mimic 8-OH-DPAT, the in vitro efficacy of the various compds. at the 5-HT1A receptor was detd. by measuring inhibition of forskolin-stimulated adenylate cyclase activity in hippocampal membranes. For a series of drugs (gepirone, ipsapirone, flexinokan, buspirone, tandospirone, yohimbine, L 657,743 and rauwolfscine) inhibition of forskolin-stimulated adenylate cyclase activity was obsd., and these same drugs showed complete cross generalization. However, RMY 14802 and MDL 73005EF did not alter adenylate cyclase activity, yet completely mimicked the stimulus properties of 8-OH-DPAT. Eltoprazine showed efficacy in inhibiting forskolin-stimulated adenylate cyclase activity, but only 30% of the responses following administration of this drug were on the 8-OH-DPAT-appropriate lever. Furthermore, although indorenate inhibited hippocampal adenylate cyclase activity, the behavioral response to this compd. was indistinguishable from the saline control. The present study indicates that activation of the 5-HT1A receptor neg. coupled to adenylate cyclase is neither necessary nor sufficient for a receptor ligand to mimic the stimulus properties of

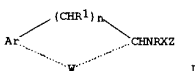
L14 ANSWER 159 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 8-OH-DPAT.
 IT 21102-95-4, EMY 7378
 RL: BIOL (Biological study)
 (serotonin 51A receptor affinity of,
 hydroxy(dipropylamino)tetralin
 action in relation to)
 RN 21102-95-4 CAPLUS
 CN 8-Azaaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

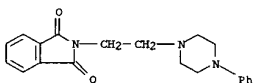
L14 ANSWER 160 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1993:225698 CAPLUS
 DOCUMENT NUMBER: 118:225698
 TITLE: Preparation of .sigma. receptor ligands as drugs
 for
 treatment of central nervous system disorders
 INVENTOR(S): Glennon, Richard A.
 PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
 SOURCE: PCT Int. Appl., 190 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 9300313 | A2 | 19930107 | WO 1992-US5330 | 19920626 |
| WO 9300313 | A3 | 19930304 | | |
| W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD | | | | |
| RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, SN, TD, TG | | | | |
| US 6057371 | A | 20000502 | US 1992-894771 | 19920610 |
| CA 2111957 | AA | 19930107 | CA 1992-2111957 | 19920626 |
| AU 9222945 | A1 | 19930125 | AU 1992-22945 | 19920626 |
| AU 676993 | B2 | 19970410 | | |
| ZA 9204775 | A | 19930416 | ZA 1992-4775 | 19920626 |
| EP 591426 | A1 | 19940413 | EP 1992-914789 | 19920626 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE | | | | |
| JP 06509069 | T2 | 19941013 | JP 1992-501248 | 19920626 |
| PRIORITY APPLN. INFO.: US 1991-720173 19910627 | | | | |
| US 1992-894771 19920610 | | | | |
| WO 1992-US5330 19920626 | | | | |
| OTHER SOURCE(S): MARPAT 118:225698 | | | | |
| GI | | | | |



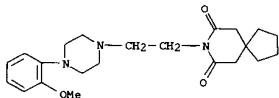
AB The phenylalkylamines, aminotetralins, piperazines, and piperidines I
 (Ar = (un)substituted aryl or heteroaryl; R = H, alkyl; R1 = R, alkoxy, chloro, etc.; RR1 = morpholino, piperazinyl, piperidinyl; W = (CH2)p,
 -H H-; X = (CH2)q, (CH2)rC.tpbond, (CH2)r, etc.; Z = H, cycloalkyl, aryl, etc.; n = 0-5; p = 1-3; q = 1-6; r = 0-3] are prepd. as selective .sigma.-receptor-binding agents, useful for the treatment of gastroenteral

L14 ANSWER 160 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 and central nervous system disorders and drug abuse. Since I do not
 bind to dopaminergic, PCP and 5-HT1A receptors, they are free of the side
 effects of the conventional neuroleptic agents. The reaction of
 R-(-)-amphetamine with 2-phenoxyethyl chloride, at 95.degree., gave
 R-(-)-N-(2-phenoxyethyl)-1-phenyl-2-aminopropane-HCl. The .sigma.-,
 PCP-, and dopamine-receptor binding assays were carried out by the method
 of Weber et al. (1986), using guinea pig brain membrane homogenates and
 the radioligand [3H]di-o-tolylguanidine.
 IT 75000-24-7
 RL: BIOL (Biological study)
 (central nervous and gastrointestinal agent, as sigma receptor
 ligand)
 RN 75000-24-7 CAPLUS
 CN 1H-Isindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-
 (9CI) (CA INDEX NAME)



L14 ANSWER 161 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1993:94851 CAPLUS
 DOCUMENT NUMBER: 118:94851
 TITLE: Allosteric interactions between the binding sites
 of
 receptor agonists and guanine nucleotides: A
 comparative study of the 5-hydroxytryptamine1A and
 adenosine A1 receptor systems in rat hippocampal
 membranes
 AUTHOR(S): Mahle, Cathy D.; Wiener, Harvey L.; Yocca, Frank
 D.;
 CORPORATE SOURCE: Mount Sinai Sch. Med., City Univ. New York, New
 York,
 NY, USA
 SOURCE: J. Pharmacol. Exp. Ther. (1992), 263(3), 1275-84
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The ternary complex formed between agonist, receptor, and guanine
 nucleotide-binding protein and its destabilization by guanine
 nucleotides
 (GN) were utilized to study early events in signal transduction, by
 characterizing the allosteric interactions between agonist and GN
 binding
 to the receptor/guanine nucleotide-binding protein, G complex for
 adenosine A1 and 5-HT1A receptors. The functional interaction
 between the
 ternary complex and GTP was examd. by assaying adenylyl cyclase
 activity.
 Binding of a full adenosine A1 agonist ([3H]-R-(-)-N6-(2-
 phenylisopropyl)adenosine) and a full ((+)-)-[3H]-8-
 hydroxydipropylaminotetralin ([3H]I) and partial ([3H]-8-[2-[4-(2-
 methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4.5]-decane-7,9-dione)
 ([3H]II) 5-HT1A agonist was examd. in relation to the binding of GN.
 The
 amt. of ternary complex formed depended upon receptor type and drug
 relative efficacy. The ratio between the drug's EC50 value (adenylyl
 cyclase) and disocn. const. (Kd) was also receptor and drug relative
 efficacy dependent. 5'-Guanylimidodiphosphate (100 .mu.M) caused an
 apprx.50% decrease in the Bmax for all drugs without affecting Kd
 values.
 5'-Guanylimidodiphosphate and guanosine 5'-O-(3-thiotriphosphate)
 attenuated [3H]-agonist binding in a concn.-dependent and saturable
 manner, with IC50 values increased 2-6-fold with increasing receptor
 occupancy. IC50 values were approx. one-tenth lower at the 5-HT1A
 receptor than at the adenosine A1 receptors; similar values were
 obtained
 for inhibition of [3H]I and [3H]II binding, suggesting an
 independence of
 agonist efficacy. It is proposed that the stabilization of the
 ternary
 complex by hormone binding, measured by Bmax values, is related to
 drug-relative efficacy; thus, the amt. of ternary complex available
 for
 destabilization by GN is greater for the more efficacious agonist.
 This

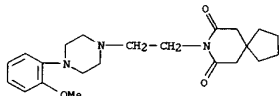
L14 ANSWER 161 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 is translated into greater relative efficacy obsd. in the maximal
 inhibition of adenylyl cyclase.
 IT 21102-95-4, RMY 7378
 RL: BIOL (Biological study)
 (serotonergic 5IA receptor binding of, in hippocampus,
 allosteric interactions between binding sites of receptor agonist and guanine
 nucleotides in relation to)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

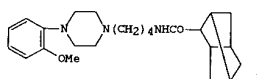
L14 ANSWER 162 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1993:32850 CAPLUS
 DOCUMENT NUMBER: 118:32850
 TITLE: Yohimbine as a serotonergic agent: evidence from
 receptor binding and drug discrimination
 Winters, J. C.; Rabin, Richard A.
 CORPORATE SOURCE: Sch. Med. Biomed. Sci., State Univ. New York,
 Buffalo,
 NY, USA
 SOURCE: J. Pharmacol. Exp. Ther. (1992), 263(2), 682-9
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Stimulus control was established in rats trained to discriminate
 either
 (3 8-hydroxy-2-(di-n-propylamino)tetralin (DPAT) (0.2 mg/kg or yohimbine
 mg/kg) from saline. Tests of generalization were then conducted with
 a group of drugs thought to act via the 5-hydroxytryptamine1A (5-HT1A)
 receptor and a group to drugs thought to act as antagonists at
 alpha.2-adrenoceptors. In addn., each drug was characterized in
 terms of its affinity for 5-HT1A and .alpha.2- adrenoceptors by means of
 radioligand binding techniques. It was obsd. that the stimulus
 effects of DPAT generalized fully to those of the .alpha.2-adrenoceptor
 antagonists, yohimbine, rauwolfscine and L-657,743, but not to idazoxan or
 atipamezole. The dissocn. consts. (Kd, nM) of the .alpha.2-adrenoceptor
 antagonists at the 5-HT1A receptor were 74, 52, 80, 199 and 13,000, resp. Thus, the
 discrimination data are explicable in terms of a direct action of
 yohimbine and some other .alpha.2-adrenoceptor antagonist upon 5-HT1A
 receptors. In yohimbine-trained rats, full generalization to DPAT,
 flesinoxan and tandospirone was obsd. In light of the negligible
 affinity of flesinoxan and tandospirone for the .alpha.2-adrenoceptor (9000 and
 8800 nM, resp.), and high affinity for the 5-HT1A receptor (0.3 and
 43 nM, resp.), a mechanism mediated by the latter site is suggested. The
 present data suggest that rats trained with yohimbine as a discriminative
 stimulus generalize to drugs with minimal affinity for the
 .alpha.2-adrenoceptor but with high affinity for 5-HT1A receptors. Studies in which
 yohimbine is used to assess the function of the .alpha.2-adrenoceptor should
 also consider the possible involvement of 5-HT1A receptors.
 IT 21102-95-4, RMY7378
 RL: BIOL (Biological study)
 (yohimbine binding to serotonergic 5IA and .alpha.2-adrenergic
 receptors response to)
 RN 21102-95-4 CAPLUS

L14 ANSWER 162 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

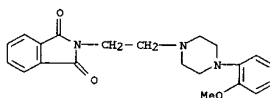


●2 HCl

L14 ANSWER 163 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1992:626102 CAPLUS
 DOCUMENT NUMBER: 117:226102
 TITLE: 4-[4-(1-Noradamantanecarboxamido)butyl]-1-(2-
 methoxyphenyl)piperazine: a high-affinity
 5-HT1A-selective agent
 El-Bermawy, Mohamed; Raghupathi, Reva; Ingber,
 Stacy
 P.; Teitler, Milt; Maayani, Saul; Glennon,
 Richard A.
 CORPORATE SOURCE: Dep. Med. Chem., Med. Coll. Virginia, Richmond,
 VA,
 23298, USA
 SOURCE: Med. Chem. Res. (1992), 2(2), 86-95
 CODEN: MCREEB; ISSN: 1054-2523
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI

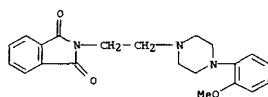


AB A problem with many arylpiperazine 5-HT1A ligands is their high
 affinity for .alpha.1-adrenergic, D2 dopamine, and/or 5-HT2 serotonin
 receptors. The title compd. (I) binds with very high affinity at 5-HT1A
 receptors (Ki = 0.1 nM) and with 460- 260- and 400-fold selectivity over
 .alpha.1-adrenergic, D2, and 5-HT2 receptors, resp. Preliminary
 studies indicate that I is a 5-HT1A partial agonist (intrinsic activity = 0.4)
 with 140-fold the affinity of the std. agent buspirone.
 IT 99718-67-9P 144391-85-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as high affinity 5-HT1A-selective agent)
 RN 99718-67-9 CAPLUS
 CN 1H-Indole-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-
 (9CI) (CA INDEX NAME)



L14 ANSWER 163 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 144391-85-5 CAPLUS
CN 1H-Indole-1,3(2H)-dione,
2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-
monohydrochloride (9CI) (CA INDEX NAME)

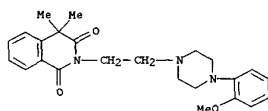


• HCl

L14 ANSWER 164 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1992:605626 CAPLUS
DOCUMENT NUMBER: 117:205626
TITLE: The .alpha.2-adrenoceptors of the human
retinoblastoma
cell line (Y79) may represent an additional
example of
the .alpha.2C-adrenoceptor
AUTHOR(S): Gleason, Marie M.; Hieble, J. Paul
CORPORATE SOURCE: Dep. Pharmacol., SmithKline Beecham Pharm., King
of
Prussia, PA, 19406, USA
SOURCE: Br. J. Pharmacol. (1992), 107(1), 222-5
CODEN: BJPCRM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB In agreement with the literature, correlation of the ability of a
series
of agonists and antagonists to displace [3H]rauwolscine binding shows
the
.alpha.2-adrenoceptors of HT29 cells, NG108-15 cells, OK cells, and
homogenates of rat sublingual gland to represent 4 distinct subtypes.
[3H]rauwolscine also bound with high affinity (KD = 0.30 nM) to a
human
retinoblastoma cell line (Y79). Specific binding represents 73% of
total
binding, and a Bmax of 38 fmol/mg protein was detd. Correlation of
antagonist affinities against [3H]rauwolscine with corresponding
values in
the other 4 tissue sources showed the Y79 cells to resemble most
closely
the OK cells, the prototype example of an .alpha.2C-adrenoceptor,
with a
correlation coeff. of 0.90 and a regression slope of 1.01 being
obtained
for 10 antagonists in these two systems. Comparison of KD values for
[3H]rauwolscine also showed a similarity between the OK cells (0.19
nM)
and Y79 cells. These data suggest that the human retinoblastoma cell
line
may represent an addnl. example of the .alpha.2C-adrenoceptor subtype.
IT 67339-62, ARC 239
RL: BIOL (Biological study)
(rauwolscine binding by various .alpha.2-adrenoceptor subtypes
inhibition by)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

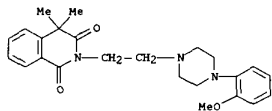
L14 ANSWER 164 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 165 OF 263 CAPLUS COPYRIGHT 2002 ACS

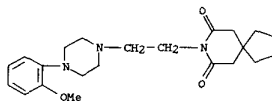
ACCESSION NUMBER: 1992:543163 CAPLUS
DOCUMENT NUMBER: 117:143163
TITLE: .alpha.2 Adrenoceptor and
catecholamine-insensitive
binding sites for [3H]rilmenidine in membranes
from
rat cerebral cortex
AUTHOR(S): King, Paul R.; Gundlach, Andrew L.; Jarrott,
Bevyn;
Louis, William J.
CORPORATE SOURCE: Clin. Pharmacol. Ther. Unit, Austin Hosp.,
Heidelberg,
3084, Australia
SOURCE: Eur. J. Pharmacol. (1992), 218(1), 101-8
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The kinetic and pharmacol. characteristics of the binding of the
oxazoline
antihypertensive drug, [3H]rilmenidine, to membranes of rat cerebral
cortex have been detd. Computerized resolu. of curvilinear, equil.
binding isotherms was consistent with the existence of two distinct
binding sites for [3H]rilmenidine: Kd 17.3 +/- 7.41 nM, Bmax 0.197
+/-
0.06 pmol/mg protein and Kd 254 +/- 48 nM, Bmax 1.59 +/- 0.08
pmol/mg
protein. Moreover, the resolu. of two assocn. and disassocn. rates also
suggested the existence of two binding site populations. Drug
inhibition
studies revealed that specific binding of [3H]rilmenidine (2 nM) was
only
inhibited by a max. of 50% by the catecholamines, adrenaline and
noradrenaline, but was completely inhibited by some oxazolines, by
guanabenz (a guanidino drug) and by several imidazoline compds.
including
naphazoline, oxymetazoline and clonidine. Binding isotherms for these
drugs were also best fit by a two-site model. The relative Ki values
at
the high affinity site for [3H]rilmenidine and the no. of these high
affinity sites are consistent with this site being an .alpha.2-
adrenoceptor. The high affinity of oxymetazoline and low affinity of
prazosin for high affinity [3H]rilmenidine binding sites together
with the
rank order of potency of oxymetazoline > phentolamine > SKF 104078 >
ARC-239 > prazosin suggest that [3H]rilmenidine binds to the .alpha.2A
sub-type of adrenoceptor. Computer-resolved Ki values for drugs at
the
larger no. of lower affinity binding sites were very similar to Ki
values
detd. in the presence of 10 .mu.M adrenaline (used to block
.alpha.2-adrenoceptor binding). The catecholamine-insensitive binding
site did not share the pharmacol. characteristics of previously
described,
high affinity imidazoline-guanidinium receptive sites or high affinity
imidazole sites, but more closely resembles the so-called "idazoxan
receptor".

L14 ANSWER 165 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 IT 67339-62-2, ARC-239
 RL: PRP (Properties)
 (affinity of, for rilmenidine binding sites in cerebral cortex)
 RN 67339-62-2 CAPLUS
 CN 1,3-(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 166 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1992:524363 CAPLUS
 DOCUMENT NUMBER: 117:124363
 TITLE: Discriminative stimulus effects of 8-OH-DPAT in pigeons: antagonism studies with the putative
 5-HT1A receptor antagonists RMY 7378 and NAN-190
 AUTHOR(S): Barrett, James E.; Gleason, Suzanne
 CORPORATE SOURCE: Med. Res. Div., American Cyanamid Co., Pearl River, NY, 10965, USA
 SOURCE: Eur. J. Pharmacol. (1992), 217(2-3), 163-71
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Pigeons were trained to discriminate 0.3 mg/kg of the 5-HT1A receptor agonist 8-hydroxy-2-(di-N-propylamino)tetralin (8-OH-DPAT) from saline.
 RU 24969 (5-methoxy-3-(1,2,3,6-tetrahydropyridin-4-yl)-1H-indole), at doses of 5.6-10 mg/kg, and eltopazine (5.6 mg/kg), both mixed 5-HT1A/B agonists, substituted completely for 8-OH-DPAT, whereas 3.0-10 mg/kg of the 5-HT 1B/C agonist TFMPP (1-(m-trifluoromethylphenyl)piperazine) and 0.1-3.0 of the 5-HT3 antagonist MDL 72222 (3-tropanyl-3,5-dichlorobenzoate) yielded only saline-appropriate responses.
 Substitution for 8-OH-DPAT by eltopazine and RU 24969, which does not occur in rats, provides in vivo support for the suggestion that the absence of a 5-HT1B receptor in the pigeon allows more complete expression of 5-HT1A-mediated effects. RMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]8-azaspiro[4.5]decane-7,9-dione) attenuated the 8-OH-DPAT stimulus at doses from 1.0 to 10 mg/kg but, when administered alone, also resulted in approx. 40% 8-OH-DPAT-appropriate responding at the highest dose.
 NAN-190 (1-(2-methoxyphenyl)-4-[4-(2-phthalamido)butyl]-piperazine (0.3-3.0 mg/kg) produced a dose-dependent and complete antagonism of the 8-OH-DPAT-discriminative stimulus: administered alone NAN-190 resulted only in saline-key responding. NAN-190 also reversed the rate-decreasing effects of higher doses of 8-OH-DPAT. The .beta.-adrenoceptor antagonist (+/-)-pindolol (5.6-17 mg/kg) antagonized the discriminative stimulus effects of lower 8-OH-DPAT doses but was unable to block the effects of higher doses of 8-OH-DPAT. Prazosin (1.0-10 mg/kg), which like NAN-190, is an .alpha.1-antagonist, neither substituted for nor blocked the discriminative stimulus effects of 8-OH-DPAT. These results suggest that NAN-190 is an effective 5-HT1A receptor antagonist in this procedure with

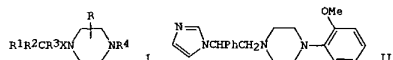
L14 ANSWER 166 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 pigeons with no indication of agonist actions, whereas RMY 7378 and pindolol are best characterized as partial 5-HT1A receptor agonists.
 IT 21102-95-4, RMY 7378
 RL: BIOL (Biological study)
 (serotonergic S1A partial agonism by, in pigeons)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

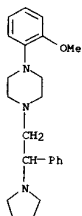
L14 ANSWER 167 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1992:490321 CAPLUS
 DOCUMENT NUMBER: 117:90321
 TITLE: Piperazine derivatives
 INVENTOR(S): Ward, Terence James; Warrillow, Graham John
 PATENT ASSIGNEE(S): John Wyeth and Brother Ltd., UK
 SOURCE: Eur. Pat. Appl., 16 pp.
 CODEN: EFKKDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|------------------|-----------------|------------|
| EP 479546 | A2 | 19920408 | EP 1991-308969 | 19911001 |
| EP 479546 | A3 | 19920603 | | |
| EP 479546 | B1 | 19961030 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GR, IT, LI, LU, NL, SE | | | | |
| AU 9184883 | A1 | 19920409 | AU 1991-84883 | 19910930 |
| AU 642532 | B2 | 19931021 | | |
| US 5177078 | A | 19930105 | US 1991-768147 | 19910930 |
| GB 2248616 | A1 | 19920415 | GB 1991-20856 | 19911001 |
| GB 2248616 | B2 | 19940615 | | |
| JP 04257570 | A2 | 19920911 | JP 1991-253585 | 19911001 |
| AT 144772 | E | 19961115 | AT 1991-308969 | 19911001 |
| ES 2094204 | T3 | 19970116 | ES 1991-308969 | 19911001 |
| CA 2052619 | AA | 19920404 | CA 1991-2052619 | 19911002 |
| HU 59394 | A2 | 19920528 | HU 1991-3160 | 19911003 |
| HU 217813 | B | 20000428 | | |
| IL 101166 | A1 | 20000813 | IL 1992-101166 | 19920306 |
| PRIORITY APPLN. INFO.: | | | GB 1990-21453 | A 19901003 |
| OTHER SOURCE(S): | | MARPAT 117:90321 | | |
| G1 | | | | |

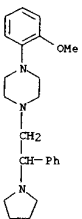


AB Piperazines I (X = alkylene; R = H, alkyl; R1, R4 = aryl, heteroaryl; R2 = mono- or bicyclic heterocyclic; R3 = H, OH, alkyl) were prepd. Thus, 1-(2-methoxyphenyl)piperazine was treated with styrene oxide followed by imidazole to give the piperazine II. II had 5-hydroxytryptamine type 1A receptor antagonist activity in rats at a min. ED of 1 mg/kg s.c. and 10 mg/kg orally.
 IT 141733-67-7P 142234-29-5P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

L14 ANSWER 167 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 141733-67-7 CAPLUS
CN Piperazine, 1-(2-methoxyphenyl)-4-[2-phenyl-2-(1-pyrrolidinyl)ethyl]-
(9CI) (CA INDEX NAME)

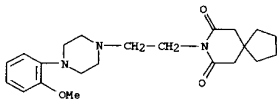


RN 142234-29-5 CAPLUS
CN Piperazine,
1-(2-methoxyphenyl)-4-[2-phenyl-2-(1-pyrrolidinyl)ethyl]-,
dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

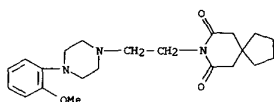
L14 ANSWER 168 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

L14 ANSWER 168 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:483356 CAPLUS
DOCUMENT NUMBER: 117:83356
TITLE: Evidence for postsynaptic mediation of the
hypothermic
effect of 5-HT1A receptor activation
AUTHOR(S): O'Connell, M. T.; Sarna, G. S.; Curzon, G.
CORPORATE SOURCE: Dep. Neurochem., Inst. Neurol., London, WC1N 3BG,
UK
SOURCE: Br. J. Pharmacol. (1992), 106(3), 603-9
CODEN: BJPCRM; ISSN: 0007-1188
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 5-HT1A ligand RMY 7378
(8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]8-
azaspiro [4,5]-decane-7,9-dione dihydrochloride, 0.032-2 mg kg-1,
s.c.)
caused hyperphagia, a response to the activation of presynaptic 5-HT1A
receptors. RMY 7378 (8 mg kg-1, s.c.) and the 5-HT1A agonist
(8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT), 0.10 and 0.25 mg
kg-1 s.c.) also caused hypothermia. This was inhibited by
(-)-pindolol (1
mg kg-1, i.p.) and not prevented by pretreatments with
p-chlorophenylalanine which grossly depleted 5-hydroxytryptamine
(5-HT)
from terminal regions. The hypothermic effects are explicable by
activation of postsynaptic 5-HT1A receptors. Infusion of RMY 7378
(8-64
.mu.g) into the dorsal raphe was without convincing hypothermic
effect.
RMY 7378 (8 mg kg-1, s.c.) inhibited another effect of activation of
postsynaptic 5-HT1A receptors, i.e., the induction of components of
the
5-HT syndrome by 8-OH-DPAT (0.5, 1.0 mg kg-1, s.c.) which suggests
that
RMY 7378 has antagonistic as well as agonistic effects at these sites.
Partial agonist properties of RMY 7378 at postsynaptic sites were also
indicated by doses for hypothermia being much greater than those for
hyperphagia i.e., ED50 (hypothermia)>2 mg kg-1, ED50 (hyperphagia) =
0.010
mg kg-1. This contrasts with the similar ED50 values for both the
hypothermic (ED50 = 0.08-0.10 mg kg-1) and hyperphagic (ED50 =
0.06-0.10
mg kg-1) effects of 8-OH-DPAT. The evidence obtained for mediation
of the
hypothermic response to 5-HT1A agonists by postsynaptic sites is
relevant
to the interpretation of the effect on it of antidepressant
treatments and
depressive illness.
IT 21102-95-4, RMY 7378
RL: PRP (Properties)
(hypothermic and hyperphagic and behavioral effects of,
serotonergic
51A receptors in relation to)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 169 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1992:420443 CAPLUS
DOCUMENT NUMBER: 117:20443
TITLE: The putative 5-HT1A antagonist RMY 7378 blocks
8-OH-DPAT-induced changes in local cerebral
glucose
utilization in the conscious rat
Graham-Smith, D.
CORPORATE SOURCE: Univ. Dep. Clin. Pharmacol., Radcliffe Infirm.,
Oxford, OX2 6HE, UK
SOURCE: Neuropharmacology (1992), 31(6), 547-51
CODEN: NEUPHW; ISSN: 0028-3908
DOCUMENT TYPE: Journal
LANGUAGE: English
AB It has previously been shown that the 5-HT1A agonist, 8-OH-DPAT,
caused
discrete changes in cerebral glucose utilization in the rat, as
assessed
by quant. 2-deoxyglucose autoradiog. Here, the effect of the putative
5-HT1A antagonist, RMY 7378, on regional cerebral glucose utilization
was
examd., when injected alone and in rats treated with 8-OH-DPAT. In
control rats, RMY 7378 (5 mg/kg, s.c.) markedly increased glucose
utilization in the lateral habenular nucleus and moderately reduced
glucose utilization in the hippocampal formation. Pretreatment with
RMY
7378 (5 mg/kg) significantly attenuated the redns. in glucose
utilization
in the hippocampus, entorhinal, piriform and cingulate cortex,
induced by
8-OH-DPAT (0.25 mg/kg). The 8-OH-DPAT-induced increase in glucose
utilization in the copula pyramis, that is putatively assocd. with the
appearance of the 5-HT behavioral syndrome, was also blocked by RMY
7378,
as was the behavioral syndrome. In summary, RMY 7378 produced few of
the
discrete changes in cerebral glucose utilization that are seen with
8-OH-DPAT. However, many of the changes induced by 8-OH-DPAT were
reversed by RMY 7378. These data are consistent with the hypothesis
that
the effects of 8-OH-DPAT on regional cerebral glucose utilization are
mediated by 5-HT1A receptors.
IT 21102-95-4, RMY 7378
RL: BIOL (Biological study)
(8-OH-DPAT-induced brain regional glucose utilization blockade by,
serotonin 51A receptors in)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

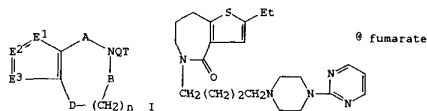


● 2 HCl

L14 ANSWER 170 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1992:194290 CAPLUS
 DOCUMENT NUMBER: 116:194290
 TITLE: Preparation of thienazepinone compounds and their use
 INVENTOR(S): Nakao, Tohru; Tanaka, Hiroshi; Yamato, Hirotake; Akagi, Takeshi; Takehara, Shuzo
 PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
 SOURCE: Eur. Pat. Appl., 74 pp.
 CODEN: EPAXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

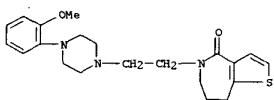
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| EP 465254 | A1 | 19920108 | EP 1991-306095 | 19910704 |
| EP 465254 | B1 | 19961113 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE | | | | |
| JP 05043582 | A2 | 19930223 | JP 1991-191087 | 19910704 |
| AT 145208 | E | 19961115 | AT 1991-306095 | 19910704 |
| CA 2046368 | AA | 19920107 | CA 1991-2046368 | 19910705 |
| US 5141930 | A | 19920825 | US 1991-726683 | 19910708 |
| PRIORITY APPL. INFO.: | | | JP 1990-179953 | 19900706 |
| | | | JP 1990-232244 | 19900831 |
| | | | JP 1990-326644 | 19901127 |
| | | | JP 1991-13684 | 19910111 |
| | | | JP 1991-75657 | 19910314 |

OTHER SOURCE(S): MARPAT 116:194290
 GI



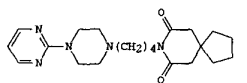
AB Title compds. I (one of E1, E2, E3 is S and the other 2 are R1C, R2C wherein R1, R2 = H, halo, O2N, H2N, cyano, HO, CHO, alkyl, alkoxy, haloalkyl, (substituted) H2SO2, alkylthio, HO2C, etc.; D = CH2, S(O)m wherein m = 0-2; Q = alkylene; T = amino, heterocyclyl; A = CO, CS, CH2; B = CO, CS) or a salt thereof, useful as antianxiotics, antipsychotics and for treatment of circulatory disorders, are prepd.
 2-Acetyl-5-[4-(2-pyrimidinyl)-1-piperazinyl]butyl-5,6,7,8-tetrahydro-4H-thieno[3,2-c]azepin-4-one (prepn. given) in F3CCO2H was added Et3SiH, the mixt. stirred for 20

L14 ANSWER 170 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 h at room temp to give after work-up and addn. of fumaric acid the thienazepinone II. In the receptor binding test, the Ki (nM) of II for 5-HT1A, 5-HT2, and D2 was 1.3, 990.0 and 78.0, resp., and the anxiolytic effect was (min. ED) .1 to req. 1.0 mg/kg, p.o. Addn. I were prepd. and tested. A tablet formulation comprising I is given.
 IT 140217-04-5P
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of, as drug)
 RN 140217-04-5 CAPLUS
 CN 4H-Thieno[3,2-c]azepin-4-one, 5,6,7,8-tetrahydro-5-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

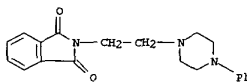


● HCl

L14 ANSWER 171 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1992:193385 CAPLUS
 DOCUMENT NUMBER: 116:193385
 TITLE: Unexpected configuration of molecules of buspirone and its analogs in solution
 AUTHOR(S): Bondarev, M. L.; Kalyuskii, A. R.; Shapiro, Yu. E.; Andronati, S. A.
 CORPORATE SOURCE: Fiz.-Khim. Inst., Odessa, USSR
 SOURCE: Ukr. Khim. Zh. (Russ. Ed.) (1991), 57(9), 986-91
 CODEN: UKZHAU; ISSN: 0041-6045
 DOCUMENT TYPE: Journal
 LANGUAGE: Russian
 GI

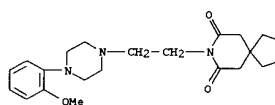


AB NMR results for buspirone (I) and several analogs in CD2Cl2, including spin-lattice relaxation times and Overhauser effects, indicated that a nearly chelate structure was preferred, possibly because of dipole-dipole interaction.
 IT 75000-24-7
 RL: FRF (Properties) (conformation of, NMR in relation to)
 RN 75000-24-7 CAPLUS
 CN 1H-Indole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 172 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1992:143745 CAPLUS
 DOCUMENT NUMBER: 116:143745
 TITLE: Antagonism studies with BMY-7378 and NAN-190:
 effects on 8-hydroxy-2-(di-n-propylamino)tetralin-induced increases in punished responding of pigeons
 AUTHOR(S): Ahlers, Stephen T.; Weissman, Ben Avi; Barrett, James
 CORPORATE SOURCE: E. Neurochem. Div., Nav. Med. Res. Inst., Bethesda, MD, USA
 SOURCE: J. Pharmacol. Exp. Ther. (1992), 260(2), 474-81
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The purported serotonin (5-HT)1A antagonists BMY-7378 and NAN-190 were examd. in pigeons for their potential to block the effects of the prototypical 5-HT1A agonist 8-OH-DPAT on punished ("conflict") and unpunished behavior and for their binding affinity at the 5-HT1A receptor site labeled by [3H]-8-OH-DPAT. Although BMY-7378 and NAN-190 both displayed high affinity for the 5-HT1A receptor (IC50 values of 0.8 and 7.5 nM, resp.), their effects, when administered alone, as well as in combination with 8-OH-DPAT, were distinct. 8-OH-DPAT (0.3-3.0 mg/kg) produced large increases in punished responding at doses that did not affect or that decreased unpunished responding. Administration of NAN-190 (1.0-3.0 mg/kg) did not increase punished responding, whereas BMY-7378 (1.0-5.6 mg/kg) slightly increased behavior suppressed by punishment. Pretreatment with BMY-7378 attenuated the rate-increasing effects of 8-OH-DPAT on punished responding; however, these effects were accompanied by dose-dependent enhancement of the rate-decreasing effects of 8-OH-DPAT on unpunished responding. In contrast, NAN-190 blocked the rate-increasing effects of 8-OH-DPAT on punished responding and also reversed the rate-decreasing effects of 8-OH-DPAT on responding that was not punished. Pretreatment with NAN-190 failed to block increases in punished responding produced by 0.1 to 1.9 mg/kg of the benzodiazepine midazolam. These data suggest that NAN-190 may be characterized as an antagonist and BMY-7378 a partial agonist with respect to 5-HT1A-induced behavioral changes obsd. in the conflict procedure with pigeons.
 IT 21102-95-4, BMY-7378
 RL: BIOL (Biological study)
 brain (serotonergic 51A receptor binding by, as partial agonist, in cerebrium, conflict behavior response to)
 RN 21102-95-4 CAPLUS

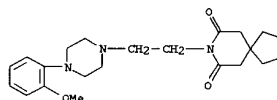
L14 ANSWER 172 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 173 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1992:143743 CAPLUS
 DOCUMENT NUMBER: 116:143743
 TITLE: The putative 5-HT1A receptor antagonists NAN-190 and BMY 7378 are partial agonists in the rat dorsal raphe nucleus in vitro.
 AUTHOR(S): Greuel, Joachim M.; Glaser, Thomas
 CORPORATE SOURCE: Inst. Neurobiol., Troponwerke G.m.b.H. und Co. K.-G., Cologne, D-5000/80, Germany
 SOURCE: Eur. J. Pharmacol. (1992), 211(2), 211-19
 CODEN: EUPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The present electrophysiol. study examd. the actions of the putative 5-HT1A receptor antagonists, NAN-190 (1-(2-methoxyphenyl)-4-[4-(2-phthalimido)butyl]piperazine-HBr) and BMY 7378 (8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-8-azaspiro[4.5]dione-7,9-dione-2HCl) in the rat dorsal raphe nucleus in vitro. There was no major difference between the effects of the two drugs on any measure investigated. Both compds. reduced neuronal activity in a concn.-dependent manner, with BMY 7378 being slightly more potent than NAN-190. The threshold concns. eliciting inhibitory effects were 1 nM for BMY 7378 and 3 nM for NAN-190. Complete inhibition occurred at concns. close to 30 nM. The effects of the 5-HT1A receptor agonist 8-OH-DPAT (8-hydroxy-2-(di-n-propylamino)tetralin) could be antagonized when concns. of NAN-190 or BMY 7378 were used that were too low to produce a marked inhibition. At concn. close to threshold both compds. potentiated the inhibitory effects of 3 nM 8-OH-DPAT. The suppression of neuronal firing induced by NAN-190 and BMY 7378 could be completely antagonized with propranolol, indicating that the inhibitory actions of both drugs were not primarily due to .alpha.1-adrenoceptor antagonism. By applying theorems of receptor theory, the intrinsic activities for both NAN-190 and BMY 7378 were calcd. to be in the range of 0.1-0.3. Thus, NAN-190 and BMY 7878 are partial agonists in the rat dorsal raphe nucleus. The results can be best explained by assuming that a crit. threshold of receptor occupancy has to be reached in order to elicit a biol. response and by assuming a receptor reserve that may account for the apparent full agonism of NAN-190 and BMY 7378.
 IT 21102-95-4, BMY 7378
 RL: BIOL (Biological study)
 of, in (serotonergic 51A antagonistic and partial agonistic activity brain dorsal raphe nucleus)

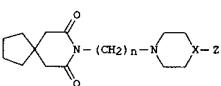
L14 ANSWER 173 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

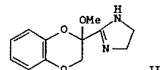
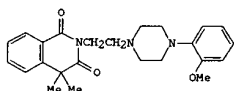
L14 ANSWER 174 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1992:41481 CAPLUS
 DOCUMENT NUMBER: 116:41481
 TITLE: Preparation of new piperazine- and piperidine-containing azaspiro[4.5]decane-7,9-dione derivatives with serotonergic activity
 INVENTOR(S): Orjales Venero, Aurelio; Rodes Solanes, Rosa
 PATENT ASSIGNER(S): Fabrica Espanola de Productos Quimicos y Farmaceuticos
 SOURCE: S. A. (FAES), Spain
 LANGUAGE: Spanish
 DOCUMENT TYPE: Patent
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|------------------|-----------------|----------|
| ES 2019228 | A6 | 19910601 | ES 1990-421 | 19900213 |
| FI 9100652 | A | 19910814 | FI 1991-652 | 19910211 |
| EP 447345 | A2 | 19910918 | EP 1991-500014 | 19910211 |
| EP 447345 | A3 | 19920415 | | |
| R: AT, BE, CH, DE, DK, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| NO 9100564 | A | 19910814 | NO 1991-564 | 19910212 |
| AU 9170983 | A1 | 19910815 | AU 1991-70983 | 19910212 |
| CA 2036269 | AA | 19910814 | CA 1991-2036269 | 19910213 |
| JP 08092221 | A2 | 19960409 | JP 1991-41144 | 19910213 |
| PRIORITY APPLN. INFO.: | | ES 1990-421 | 19900213 | |
| OTHER SOURCE(S): | | MARPAT 116:41481 | | |



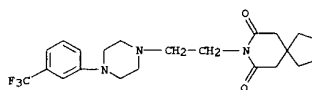
AB Title compds. I [X = N, CH; n = 2 or 4; Z = pyrimidin-2-ylamino, 3-F3CC6H4, or benzimidazol-2-yl substituted in 1-position by lower alkyl or 4-FC6H4CH2] are prepd. by cyclocondensation of 3,3-tetramethyleneglutaric anhydride (II) with corresponding amines in, e.g., pyridine, PhMe, or BuOH, at 80-140.degree., preferably at reflux temp. Thus, reaction of II with 1-(4-aminobutyl)-4-[3-(trifluoromethyl)phenyl]piperazine in refluxing pyridine over 20 h gave 66% I (X = N, n = 4, Z = 3-F3CC6H4). I showed 5-HT1A receptor activity (displacement of [3H]-8-OH-DPAT from rat frontal cortex tissue) similar to

L14 ANSWER 175 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:671300 CAPLUS
 DOCUMENT NUMBER: 115:271300
 TITLE: Delineation of three pharmacological subtypes of .alpha.2-adrenoceptor in the rat kidney
 AUTHOR(S): Uhlen, Staffan; Wikberg, Jarl E. S.
 CORPORATE SOURCE: Dep. Pharmacol., Umea Univ., Umea, S-901 87, Swed.
 SOURCE: Br. J. Pharmacol. (1991), 104(3), 657-64
 CODEN: BJPCRM; ISSN: 0007-1108
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI

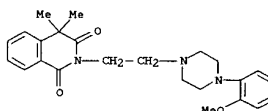


AB Simultaneous computer modeling of plain and ARC 239 (I)- and guanoxabenz-masked [3H]-RX 821002 (II) satn. curves, plain I and guanoxabenz competition curves as well as I-masked guanoxabenz competition curves revealed that the drugs bound to three .alpha.2-adrenoceptor subtypes in the rat kidney with grossly differing selectivities. These .alpha.2-adrenoceptor subtypes were termed .alpha.2A, .alpha.2B1, and .alpha.2B2. The order of affinities for [3H]II for the adrenoceptor sites was .alpha.2A > .alpha.2B1 > .alpha.2B2, the Kds being 0.62, 2.25, and 6.74 nM, resp. The order of affinities for I was .alpha.2B1 > .alpha.2B2 .mchgt. .alpha.2A with Kds 4.78, 28.8, and 1460 nM, resp. For guanoxabenz the order of affinities was .alpha.2A > .alpha.2B1 .mchgt. .alpha.2B2 with Kds 99.7, 508, and 25,400 nM, resp. The affinities of guanoxabenz for .alpha.2B1- and .alpha.2B2-adrenoceptors differed 72-fold and for .alpha.2A- and .alpha.2B2-adrenoceptors 380-fold. The selectivities of a no. of other drugs were less marked but their Kds were consistent with all 3 sites being .alpha.2-adrenoceptors. (-)-Adrenaline and (-)-noradrenaline showed dissimilar order of affinities for the three .alpha.2-adrenoceptors. For (-)-adrenaline the order of affinities was .alpha.2B1 .gtoreq. .alpha.2A > .alpha.2B2 and for (-)-noradrenaline

L14 ANSWER 174 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 buspirone (Xi = 1.99 .times. 10-8).
 IT 138307-27-4P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as nervous system agent)
 RN 138307-27-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione,
 8-[2-(4-[3-(trifluoromethyl)phenyl]-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

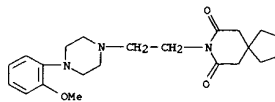


L14 ANSWER 175 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 .alpha.2B2 .gtoreq. .alpha.2B1 > .alpha.2A. All three .alpha.2-adrenoceptors showed the expected stereoselective binding for adrenaline enantiomers, the (+)-form being 7-10-fold less potent than the (-)-form. [3H]yohimbine was also used as radioligand. The data with this ligand were fully compatible with the [3H]II data. However, [3H]yohimbine appeared to label only .alpha.2B1- and .alpha.2B2-adrenoceptors presumably because it had too low an affinity for .alpha.2A-adrenoceptors. Apparently, 3 pharmacol. subtypes of .alpha.2-adrenoceptors are labeled by [3H]II in the rat kidney. Guanoxabenz and ARC 239 may be used in competition studies to delineate between these three .alpha.2-adrenoceptor subtypes.
 IT 67339-62-2, ARC-239
 RL: BIOL (Biological study)
 (.alpha.2-adrenergic receptor classification with, in kidney)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 176 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:598360 CAPLUS
 DOCUMENT NUMBER: 115:198360
 TITLE: Effects of serotonergic agents on
 isolation-induced aggression
 AUTHOR(S): White, Sheryl M.; Kucharik, Robert F.; Moyer,
 John A.
 CORPORATE SOURCE: CNS Div., Wyeth-Ayerst Res., Princeton, NJ,
 08543-8000, USA
 SOURCE: Pharmacol., Biochem. Behav. (1991), 39(3), 729-36
 CODEN: PBEHAI; ISSN: 0091-3057
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A series of serotonergic agents were assessed for their ability to
 antagonize isolation-induced aggression and disrupt performance in
 the rotorod motor coordination test. All compds. with 5-HT1A activity
 [buspirone, gepirone, ipsapirone, tandospirone (SM-3997), 8-OH-DPAT,
 Wy48,723, RMY7378, Wy47,846] reduced aggression at doses below those
 which produced debilitation in the rotorod motor coordination test. In
 addn., the 5-HT3 antagonist zacopride failed to attenuate aggression or
 produce debilitation at any of the doses tested; however, the 5-HT2
 antagonist ritanserin inhibited aggressive behavior at a high dose which was not
 debilitating. Benzodiazepines (chlordiazepoxide, diazepam and
 lorazepam), and an antidepressant (desipramine) and an antipsychotic
 (haloperidol) reduced aggressive behavior only at debilitating doses. Activity at
 the 5-HT1A receptor, and possibly non-sedative anxiolytic activity,
 appears to be related to antagonism of isolation-induced aggression.
 IT 21102-95-4, RMY-7378
 RL: BIOL (Biological study)
 (isolation-induced aggression response to, serotonergic
 mechanisms
 in)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspino[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 176 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

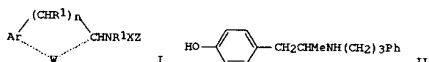
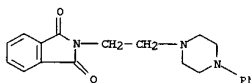


● 2 HCl

L14 ANSWER 177 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:592801 CAPLUS
 DOCUMENT NUMBER: 115:182801
 TITLE: Preparation of substituted phenylisopropylamines
 and analogs as sigma receptor ligands for treatment
 of schizophrenia and psychoses
 INVENTOR(S): Glennon, Richard A.
 PATENT ASSIGNEE(S): Virginia Commonwealth University, USA
 SOURCE: PCT Int. Appl., 101 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9109594 | A1 | 19910711 | WO 1990-057653 | 19901228 |
| W: AU, BB, BG, BR, CA, FI, HU, JP, KP, KR, LK, MC, MG, MW, NO, | | | | |
| PL, RO, SD, SU, US | | | | |
| RW: AT, BE, BF, BJ, CF, CG, CH, CM, DE, DK, ES, FR, GA, GB, GR, | | | | |
| IT, LU, ML, MR, NL, SE, SN, TD, TG | | | | |
| CA 2071897 | AA | 19910629 | CA 1990-2071897 | 19901228 |
| AU 9171684 | A1 | 19910724 | AU 1991-71684 | 19901228 |
| AU 658134 | E2 | 19950406 | | |
| EP 507863 | A1 | 19921014 | EP 1991-902640 | 19901228 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| JP 05503517 | T2 | 19930610 | JP 1991-502935 | 19901228 |
| PRIORITY APPLN. INFO.: US 1989-459061 19891228 | | | | |
| WO 1990-057653 19901228 | | | | |
| OTHER SOURCE(S): MARPAT 115:182801 | | | | |
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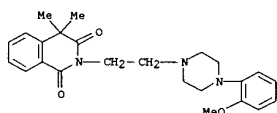
L14 ANSWER 177 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 phenyl-2-aminopropane. Also prepd. was the (+,+) -amine II.HBr
 (III). In sigma receptor binding assays the IC50 of III was 1.03 .times. 10-8
 M. I were subjected to sigma, PCP and dopamine receptor binding assays and
 the results showed very high binding to sigma receptor and very low
 binding to PCP and DA receptors, and thus I are useful for treatment of mental
 illness (no data) without the extrapyramidal side effects of
 traditional neuroleptic agents caused by binding to DA receptor.
 IT 75000-24-7p
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as sigma receptor ligand)
 RN 75000-24-7 CAPLUS
 CN 1H-Indole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI)
 (CA INDEX NAME)



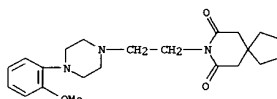
AB Title compds. I [Ar = (substituted) aryl or heteroaryl; R = H, C1-6
 alkyl;
 R1 = H, C1-6 alkyl, C1-6 alkoxy, Br, Cl, F, O, or RR1 = morpholine,
 piperazinyl, piperidinyl; n = 0-5; W = (CH2)p, 2H; p = 1-3; X =
 (CH2)q; q =
 = 1-6, (CH2)rC.tplbond.C(CH2)r, (CH2)rCH:CH(CH2)r, (CH2)rCO(CH2)r,
 (CH2)rY(CH2)r; r = 0-3; Y = O, S, C1-6 alkyl; Z = H, (substituted)
 aryl or
 heteroaryl], are prepd. PhCH2CH2CHO and (R)-(-)-PhCH2CH(NH2)Me in
 MeOH
 were hydrogenated over Pt/C at room temp. to give
 (R)-N-(3-phenylpropyl)-1-

II

L14 ANSWER 179 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:551496 CAPLUS
 DOCUMENT NUMBER: 115:151496
 TITLE: Identification and characterization of .alpha.2D-adrenergic receptors in bovine pineal gland
 AUTHOR(S): Simonneau, V.; Ebadi, M.; Bylund, D. B.
 CORPORATE SOURCE: Med. Cent., Univ. Nebraska, Omaha, NE,
 68198-6260, USA
 SOURCE: Mol. Pharmacol. (1991), 40(2), 235-41
 CODEN: MOPMA3; ISSN: 0026-895X
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB By using [3H]rauwolscine, a selective .alpha.2-adrenergic receptor antagonist, .alpha.2-adrenergic receptor sites were identified in a mammalian pineal gland. [3H]Rauwolscine bound in a saturable manner to a single class of receptors, with an equil. disocn. const. of 1.4 nM and a d. of 71 fmol/mg of protein, in crude synaptic membrane preps. from bovine pineal gland. Competition studies carried out with various adrenergic antagonists supported the conclusion that [3H]rauwolscine-binding sites were .alpha.2-adrenergic receptors. The bovine pineal .alpha.2-adrenergic receptor appears to represent a pharmacol. subtype distinct from the 3 currently proposed subtypes, i.e., .alpha.2 found in a human colonic adenocarcinoma cell line (HT29 cell) .alpha.2B found in rat lung, and .alpha.2C found in an opossum kidney cell line. However, the pharmacol. profile of the pineal .alpha.2 receptor resembles that found in the rat submaxillary gland. The bovine pineal receptor may represent a 4th pharmacol. subtype, which would be designated as .alpha.2D.
 IT 67339-62-2, ARC-239
 RL: BIOL (Biological study)
 (alpha.2D-adrenergic receptor binding by, in pineal gland)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 179 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

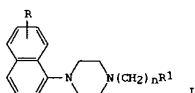


●2 HCl

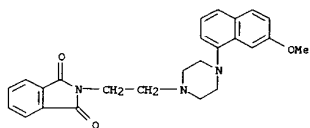
L14 ANSWER 179 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:528127 CAPLUS
 DOCUMENT NUMBER: 115:128127
 TITLE: Single-dose 8-OH-DPAT pretreatment does not induce tachyphylaxis to the 5-HT release-reducing effect of 5-HT1A autoreceptor agonists
 AUTHOR(S): Hjorth, Stephan
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Goteborg, Goteborg, S-400 33, Sweden.
 SOURCE: Eur. J. Pharmacol. (1991), 199(2), 237-42
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB It has recently been suggested that central 5-HT1A autoreceptors are already desensitized after single-dose 5-HT1A agonist treatment. In turn, this would lead to an attenuated feedback suppression of transmitter release from 5-HT neurons, and thus to enhanced 5-HT synaptic transmission. In vivo brain microdialysis techniques were used in an attempt to test this hypothesis. Single-dose pretreatment with the ref. 5-HT1A receptor agonist 8-hypoxo-2-(di-n-propylamino)tetralin, 8-OH-DPAT, did not alter the baseline output of 5-HT in the rat ventral hippocampus 24 h later, and did not alter the release-reducing response to 5-HT1A agonist (8-OH-DPAT, ipsapirone or RMY 7378) challenge under the same conditions. Thus, the functional responsiveness of the 5-HT release-controlling 5-HT1A autoreceptors is maintained after bolus 8-OH-DPAT pretreatment. When related to the acute 8-OH-DPAT-induced redn. in raphe 5-HT1A radioligand binding d. recently reported by others, the present results are consistent with a large functional overcapacity of this 5-HT1A receptor population. The mechanism by which 5-HT1A receptor-mediated hypothermia and hyperphagia are rapidly attenuated by a previous large single dose of a 5-HT1A receptor agonist remains to be explained.
 IT 21102-95-4, RMY 7378
 RL: BIOL (Biological study)
 (serotonin release by hippocampus response to, receptor desensitization in relation to)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 180 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:514553 CAPLUS
 DOCUMENT NUMBER: 115:114553
 TITLE: 1-naphthylpiperazine derivatives, process for their preparation and pharmaceutical compositions containing them
 INVENTOR(S): Lavielle, Gilbert; Laubie, Michel; Colpaert, Francis
 PATENT ASSIGNEE(S): ADIR et Cie., Fr.
 SOURCE: Eur. Pat. Appl., 58 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-------------------|----------|
| EP 434561 | A2 | 19910626 | EP 1990-403688 | 19901220 |
| EP 434561 | A3 | 19910918 | | |
| EP 434561 | B1 | 19951018 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE | | | | |
| FR 2655988 | A1 | 19910621 | FR 1989-16882 | 19891220 |
| FR 2655988 | B1 | 19940520 | | |
| ZA 9009767 | A | 19911127 | ZA 1990-9767 | 19901205 |
| CA 2032713 | AA | 19910621 | CA 1990-2032713 | 19901219 |
| AU 9068235 | A1 | 19910627 | AU 1990-68235 | 19901219 |
| AU 635369 | B2 | 19930318 | | |
| JP 03291275 | A2 | 19911220 | | |
| JP 06076395 | B4 | 19940528 | JP 1990-403922 | 19901219 |
| US 5143916 | A | 19920901 | US 1990-629824 | 19901219 |
| AT 129241 | E | 19951115 | AT 1990-403688 | 19901220 |
| ES 2080815 | T3 | 19960216 | ES 1990-403688 | 19901220 |
| US 5166157 | A | 19921124 | US 1991-750821 | 19910827 |
| US 5162324 | A | 19921110 | US 1991-752060 | 19910829 |
| US 5162321 | A | 19921110 | US 1991-752063 | 19910829 |
| US 5166156 | A | 19921124 | US 1991-752065 | 19910829 |
| PRIORITY APPLN. INFO.: | | | FR 1989-16882 | 19891220 |
| | | | US 1990-629824 | 19901219 |
| OTHER SOURCE(S): | | | MARPAT 115:114553 | |
| GI | | | | |



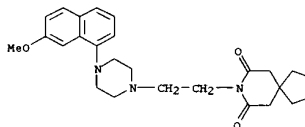
L14 ANSWER 180 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 AB Naphthylpiperazines I [n = 1-4; R = H, halogen, OH, alkyl, alkoxy;
 R1 = NHCOR2, NHO2R3, NHCONHR4, (un)substituted phthalimido,
 benzisothiazole
 dioxide, NBz2, imidazopyrimidinyl, azaspirodecyl; R2 = alkyl,
 cycloalkyl,
 Ph, substituted Ph, heteroaryl; R3 = alkyl, cycloalkyl, Ph,
 substituted
 Ph; R4 = alkyl, Ph, substituted Ph] were prepd. by various methods.
 Thus 7-methoxy-1-naphthylpiperazine was treated with BrCH2CN, followed by
 redn.
 to the 2-aminoethyl deriv. and acylation to give I (n = 2, R =
 7-OMe, R1 =
 4-FC6H4CONH) which had better antihypertensive and neg. chronotropic
 activity than flequinon.
 IT 135722-16-6P 135722-24-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)
 RN 135722-16-6 CAPLUS
 CN 1H-Isindole-1,3(2H)-dione, 2-[2-[4-(7-methoxy-1-naphthalenyl)-1-
 piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

RN 135722-24-6 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione,
 8-[2-[4-(7-methoxy-1-naphthalenyl)-1-
 piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

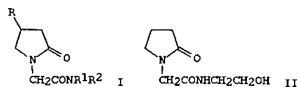
L14 ANSWER 180 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



●x HCl

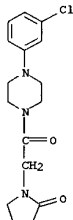
L14 ANSWER 181 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:492061 CAPLUS
 DOCUMENT NUMBER: 115:92061
 TITLE: Preparation of 2-pyrrolidone derivatives as
 enhancers
 for learning and memory
 INVENTOR(S): Giannessi, Fabio; Ghirardi, Orlando; Misiti,
 Domenico;
 PATENT ASSIGNEE(S): Tinti, Maria Ornella; Scolastico, Carlo
 Sigma-Tau Industrie Farmaceutiche Riunite S.p.A.,
 Italy
 SOURCE: Eur. Pat. Appl., 20 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| EP 408524 | A1 | 19910116 | EP 1990-830317 | 19900710 |
| EP 408524 | B1 | 19951108 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, LI, LU, NL, SE | | | | |
| AT 129396 | E | 19951115 | AT 1990-830317 | 19900710 |
| ES 2079469 | T3 | 19960116 | ES 1990-830317 | 19900710 |
| JP 03048657 | A2 | 19910301 | JP 1990-185173 | 19900711 |
| US 5061725 | A | 19911029 | US 1990-551951 | 19900712 |
| PRIORITY APPLN. INFO.: IT 1989-48180 | | | 19890712 | |
| OTHER SOURCE(S): MARPAT 115:92061 | | | | |
| GI | | | | |

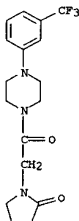


AB The title compds. I [R = H, OH; R1 = H; R2 = 2-aminoethyl,
 2-(diisopropylamino)ethyl, 2-hydroxyethyl, etc.] were prepd. A
 mixt. of
 Me (2-oxopyrrolidin-1-yl)acetate and ethanolamine was stirred at room
 temp. for 20 h to give pyrrolidone deriv. II. I (R = R1 = H; R2 =
 CH2CH2NH2) had memory-enhancing activity equal to that of piracetam.
 IT 131028-02-9P 135459-98-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as memory enhancer)
 RN 131028-02-9 CAPLUS
 CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-
 (9CI)
 (CA INDEX NAME)

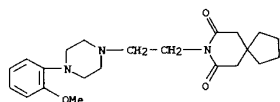
L14 ANSWER 181 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 135459-98-2 CAPLUS
 CN Piperazine,
 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-[3-(trifluoromethyl)phenyl]-
 (9CI) (CA INDEX NAME)

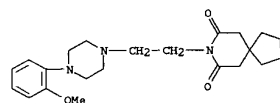


L14 ANSWER 182 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:485329 CAPLUS
 DOCUMENT NUMBER: 115:85329
 TITLE: BMY 7378 is an agonist at 5-HT1A receptors
 mediating hypotension and renal sympatho-inhibition in anesthetized cats
 AUTHOR(S): Stubbs, Carole M.; Connor, Helen E.; Fenluk, Wasyi
 CORPORATE SOURCE: Dep. Neuropharmacol., Glaxo Group Res. Ltd., Ware/Hertfordshire, SG12 0DJ, UK
 SOURCE: Eur. J. Pharmacol. (1991), 197(1), 113-16
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The putative 5-HT1A receptor antagonist BMY 7378 (3-100 .mu.g.cntdot.kg-1 i.v.) caused redns. in blood pressure, heart rate and efferent renal nerve activity in anesthetized cats. Similar effects were produced by the selective 5-HT1A receptor agonist, 8-hydroxy-2-(di-n-propylamino) tetralin (8-OH-DPAT 1-10 .mu.g.cntdot.kg-1 i.v.). The sympatho-inhibitory effects of BMY 7378 and 8-OH-DPAT, but not those of clonidine were reversed by the non-selective 5-HT1A receptor antagonist, spiperone (1 mg.cntdot.kg-1 i.v.). It is concluded that BMY 7378 is an agonist at 5-HT1A receptors mediating hypotension and renal sympatho-inhibition in anesthetized cats.
 IT 21102-95-4, BMY 7378
 RL: BIOL (Biological study)
 (as serotonergic 5HT1A receptor agonist, cardiovascular and renal sympathetic nerve response to)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 183 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 heterobicyclic arylpiperazine selective 5-HT1A ligand, (.-.-)-flesinoxan, also failed to evoke STFs and attenuated the action of 8-OH-DPAT. The novel, putative 5-HT1A antagonists, BMY 7378 and NAN 190, abolished the action of 8-OH-DPAT and p-chloroamphetamine. Thus, a high efficacy agonist action at 5-HT1A receptors is sufficient for the induction of STFs in the rat. This response offers a novel, robust, and quant. test for the in vivo characterization of drugs acting at 5-HT1A receptors.
 IT 21102-95-4, BMY 7378
 RL: BIOL (Biological study)
 (serotonergic 5HT1A agonist-induced tail flick behavior antagonism by)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

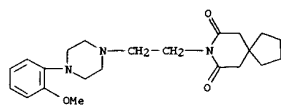


●2 HCl

L14 ANSWER 183 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:221898 CAPLUS
 DOCUMENT NUMBER: 114:221898
 TITLE: 5-Hydroxytryptamine (5-HT)1A receptors and the tail-flick response. I. 8-Hydroxy-2-(di-n-propylamino)tetralin hydrobromide-induced spontaneous tail-flicks in the rat as an in vivo model of 5-HT1A receptor-mediated activity
 AUTHOR(S): Millan, Mark J.; Bervoets, Karin; Colpaert, Francis C.
 CORPORATE SOURCE: Neurobiol. Div., Fondax, Puteaux, 92800, Fr.
 SOURCE: J. Pharmacol. Exp. Ther. (1991), 256(3), 973-82
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB This study characterizes a novel behavioral response as a potential in vivo model of 5-HT1A receptor-mediated activity. In rats restrained in horizontal cylinders, the selective 5-HT1A agonist 8-hydroxy-2-(di-n-propylamino)tetralin-HBr (8-OH-DPAT) dose-dependently (0.04-10.0 mg/kg, s.c.) elicited spontaneous tail-flicks (STFs). This action was mimicked by other ligands possessing high affinity and high efficacy at 5-HT1A sites: RU 24969, lisuride, (+)-LSD, and 5-methoxy-N,N-dimethyltryptamine hydrogen oxalate. The response could not be elicited by CGS 120668, mCPP [1-(3-chlorophenyl)-piperazine-2-HCl], TMPP, MK 212, quipazine, and (+-)-2,5-dimethoxy-4-iodophenyl-2-aminopropane-HCl, which act in vivo as agonists at 5-HT1B, 5-HT1C and/or 5-HT2 receptors, or by the 5-HT3 agonist, 2-methyl-5-HT. p-Chloroamphetamine, which releases endogenous 5-HT, also evoked STFs; in contrast, d-amphetamine, a preferential releaser of catecholamines, was inactive as were agonists and antagonists at .alpha.1-, .alpha.2-, .beta.1-, .beta.2-, and dopamine D1 and D2 sites. 8-OH-DPAT-elicited STFs were blocked by the 5-HT1/2 antagonist, methiothepin, but not by the 5-HT1C/5-HT2 antagonists, mianserin, ritanserin, and ICI 169,369 nor by the 5-HT3 antagonists, GR 38032F, ICS 205,930, and MDL 72222. .beta.-Blockers with high 5-HT1A affinity i.e., (-)-alprenolol, (+-)-isamoltane and, stereoselectively, (-)- but not (+)-pindolol, blocked the action of 8-OH-DPAT. Spiperone and spiroxatrine, D2 antagonists with high 5-HT1A affinity, also inhibited 8-OH-DPAT-induced STFs. Selective .beta.-blockers and D2 antagonists with low 5-HT1A affinity were inactive. 5-HT1A partial agonists, the pyrimidinylpiperazines buspirone, gepirone, and ipsapirone, the halogenated phenylpiperazine LY 165,163, and the benzodioxan MDL 72832 did not elicit STFs and antagonized the effect of 8-OH-DPAT. The

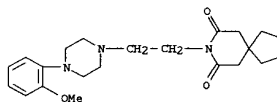
L14 ANSWER 184 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:178855 CAPLUS
 DOCUMENT NUMBER: 114:178855
 TITLE: 5-Hydroxytryptamine (HT)1A receptors and the tail-flick response. II. High efficacy 5-HT1A agonists attenuate morphine-induced antinociception in mice in a competitive-like manner
 AUTHOR(S): Millan, M. J.; Colpaert, F. C.
 CORPORATE SOURCE: Neurobiol. Div., Fondax, Puteaux, 92800, Fr.
 SOURCE: J. Pharmacol. Exp. Ther. (1991), 256(3), 983-92
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB This study examd. the influence of s.c. administration of HT1A agonists upon the antinociceptive action of s.c. injected morphine in tail-flick tests to noxious heat and pressure. The selective 5-HT1A agonist, (.-.-)-8-hydroxy-dipropylaminotetralin-Br (8-OH-DPAT), dose-dependently antagonized morphine-induced antinociception (MIA) without affecting the latency to respond when applied alone. In the presence of increasing doses of 8-OH-DPAT (0.16-0.63 mg/kg), the morphine dose-response curve was shifted progressively in parallel to the right and the maximal effect of morphine was not altered: Schild anal. yielded a slope of close to -1.0. 8-OH-DPAT both prevented and reversed the action of morphine. The action of 8-OH-DPAT was reversible (at 24 h). In contrast, 8-OH-DPAT neither blocked morphine-induced Straub tail nor pptd. withdrawal in morphine-dependent animals; thus, it lacked opioid-antagonist properties. The antagonism of MIA by 8-OH-DPAT was mimicked by addnl. drugs acting as high efficacy 5-HT1A agonists: lisuride, 5-methoxy-N,N-dimethyltryptamine hydrogen oxalate, RU 24969 and d-LSD. In contrast, the 5-HT1B/1C agonist TMPP and the 5-HT1C/2 agonist (.-.-)-2,5-dimethoxy-4-iodophenyl-2-aminopropane-HCl were ineffective. The putative selective 5-HT1A antagonists BMY 7378 and spiperone did not reduce MIA. Indeed, BMY 7378 blocked the ability of 8-OH-DPAT to antagonize MIA. Under the present conditions, agonists and antagonists at adrenergic and dopaminergic receptors did not attenuate MIA. These data show that, over a certain range of doses, the systemic administration of 8-OH-DPAT and other high efficacy 5-HT1A agonists functionally antagonizes the antinociceptive action of systemically applied morphine in a competitive-like manner.
 IT is suggested that 5-HT1A receptors play an important role in the modulation of opioidergic antinociceptive mechanisms.
 21102-95-4, BMY 7378
 RL: BIOL (Biological study)

L14 ANSWER 184 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 (serotonergic 5-HT_{1A} agonist antagonism of morphine analgesia blockade by)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 185 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:178780 CAPLUS
 DOCUMENT NUMBER: 114:178780
 TITLE: Differential behavior activation following intra-raphe infusion of 5-HT_{1A} receptor agonists
 AUTHOR(S): Higgins, Guy A.; Elliott, Peter J.
 CORPORATE SOURCE: Dep. Neuropharmacol., Glaxo Group Res. Ltd., Ware/Harfordshire, SG12 0DP, UK
 SOURCE: Eur. J. Pharmacol. (1991), 193(3), 351-6
 CODEN: EJPFAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Microinfusion of the selective 5-HT_{1A} receptor agonist, 8-hydroxy-(di-N-propylamino)tetralin (8-OHDPAT), into the dorsal raphe nucleus (DRN) produced a marked behavioral hypoactivity and flat body posture. Injections of similar doses into the median raphe nucleus (MRN) elicited hyperactivity but no postural change. Redns. in rearing and grooming were also obsd. after DRN and MRN infusions of 8-OHDPAT. The behavioral profiles of other 5-HT_{1A} selective compds., gepirone and BMV7378 were found to be similar to 8-OHDPAT. The contrasting behavioral profiles of the 5-HT_{1A} agents obsd. after DRN or MRN microinfusion are probably related to the differential innervation of forebrain structures by each raphe nucleus. Thus, the present data confirms and extends previous results illustrating the influence of 5-HT systems on motor behavior in the rat and identifies unique behavioral profiles following activation of the DRN and MRN.
 IT 21102-95-4, RMY 7378
 RL: BIOL (Biological study)
 (behavior response to intra-raphe administration of, serotonergic mechanism for)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L14 ANSWER 186 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:143444 CAPLUS
 DOCUMENT NUMBER: 114:143444
 TITLE: Preparation of 1-aryl-4-carboxyalkylpiperazines and related compounds as serotonergic antagonists
 INVENTOR(S): Cliffe, Ian Anthony
 PATENT ASSIGNEE(S): Wyeth, John, and Brother Ltd., UK
 SOURCE: Eur. Pat. Appl., 33 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

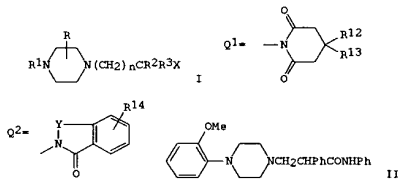
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| EP 395312 | A2 | 19901031 | EP 1990-304250 | 19900420 |
| EP 395312 | A3 | 19910508 | | |
| EP 395312 | B1 | 19990512 | | |
| CA 2015034 | AA | 19901022 | CA 1990-2015034 | 19900420 |
| AU 9053779 | A1 | 19901025 | AU 1990-53779 | 19900420 |
| AU 619678 | B2 | 19920130 | | |
| GB 2230781 | A1 | 19901031 | GB 1990-8925 | 19900420 |
| GB 2230781 | B2 | 19930428 | | |
| HU 54666 | A2 | 19910328 | HU 1990-2504 | 19900420 |
| DD 296921 | A5 | 19911219 | DD 1990-339954 | 19900420 |
| ZA 9003019 | A | 19911224 | ZA 1990-3019 | 19900420 |
| ZA 9003020 | A | 19911224 | ZA 1990-3020 | 19900420 |
| DD 297966 | A5 | 19920130 | DD 1990-339955 | 19900420 |
| IL 94151 | A1 | 19950831 | IL 1990-94151 | 19900420 |
| AT 179973 | E | 19900515 | AT 1990-304250 | 19900420 |
| ES 2130116 | T3 | 19990701 | ES 1990-304250 | 19900420 |
| JP 03011059 | A2 | 19910118 | JP 1990-106299 | 19900421 |
| JP 3036786 | B2 | 20000424 | | |
| US 5364849 | A | 19941115 | US 1992-911996 | 19920710 |
| GB 2255976 | A1 | 19921125 | GB 1992-15425 | 19920720 |
| GB 2255976 | B2 | 19921125 | | |
| US 5382583 | A | 19950117 | US 1992-998887 | 19921229 |
| US 5340812 | A | 19940823 | US 1993-1428 | 19930107 |
| US 5420278 | A | 19950530 | US 1994-248124 | 19940524 |
| US 5541326 | A | 19960730 | US 1994-339000 | 19941114 |

PRIORITY APPLN. INFO.:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----------------|------|----------|-----------------|------|
| GB 1989-9209 | A | 19890422 | | |
| GB 1989-24323 | A | 19891028 | | |
| US 1990-511150 | B2 | 19900419 | | |
| GB 1990-8925 | A3 | 19900420 | | |
| US 1991-748496 | B1 | 19910822 | | |
| US 1991-748497 | B1 | 19910822 | | |
| US 1991-756932 | B1 | 19910909 | | |
| US 1992-911996 | A3 | 19920710 | | |
| US 1992-998887 | A3 | 19921229 | | |

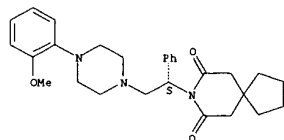
OTHER SOURCE(S): MARPAT 114:143444
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L14 ANSWER 186 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



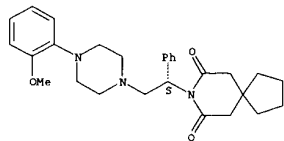
AB The title compds. [I; R = H, alkyl; R1 = aryl, N-contg. heteroaryl; R2 = H, alkyl; R3 = aryl, alkyl, arylalkyl; X = O2CR10, CO2R6, CONR5R9, OCO2R6, NR4COR6, Q1, Q2, etc.; R4 = H, alkyl; R6 = alkyl, cycloalkyl, arylalkyl; R5 = H, alkyl, cycloalkyl, aryl, arylalkyl, 8-azaspiro[4.5]deca-7,9-dione-8-yl-alkyl, etc.; R12, R13 = alkyl; R12R13 = cycloalkyl; R14 = H, halo, alkyl, alkoxy; Y = CO, SO2; n = 1, 2] were prepd. Thus, 1-(2-methoxyphenyl)piperazine was refluxed 18 h with stropic acid in EtOH to give .alpha.-[1-[4-(2-methoxyphenyl)piperazinyl]methyl]benzeneacetic acid. The latter in CH2Cl2 was treated with carbonyldiimidazole and then aniline to give title compd. II. I bound to rat hippocampal 5-HT_{1A} receptors with IC50's of 8-127 nM.
 IT 132708-63-5P 132709-11-6P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as serotonergic antagonist)
 RN 132708-63-5 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-phenylethyl]-, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

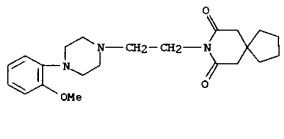


RN 132709-11-6 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione,
 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-
 1-phenylethyl]-, dihydrochloride, (S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



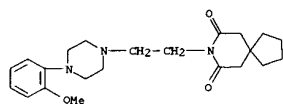
● 2 HCl



● 2 HCl

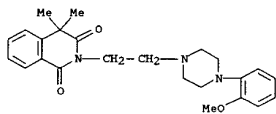
L14 ANSWER 187 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:136585 CAPLUS
 DOCUMENT NUMBER: 114:136585
 TITLE: The effect of putative 5-HT1A receptor antagonists on 8-OH-DPAT-induced hypothermia in rats and mice
 AUTHOR(S): Moser, Paul C.
 CORPORATE SOURCE: Merrell Dow Res. Inst., Strasbourg, F-67009, Fr.
 SOURCE: Eur. J. Pharmacol. (1991), 193(2), 165-72
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The effects of 3 putative 5-HT1A receptor antagonists (NAN-190, RMY 7378, and WB 4101) were studied on the hypothermia induced by 8-hydroxy-2-(dipropylamino)tetralin (8-OH-DPAT). In order to control for the .alpha.1-adrenoceptor antagonist activity of NAN-190 and WB 4101, the effects of prazosin were also examd. Both NAN-190 and WB 4101 lowered body temp. in the mouse. This effect appeared to be due to their .alpha.1-adrenoceptor antagonist effects, as prazosin had a similar profile. Neither NAN-190, WB 4101 nor prazosin antagonized the hypothermic effects of 8-OH-DPAT. RMY 7378 slightly lowered body temp. but to a lesser extent than 8-OH-DPAT and, in contrast to the other compds. studied, also prevented a fall in body temp. on injection of 8-OH-DPAT. In the rat there was much less interference from .alpha.1-adrenoceptor antagonist activity as both NAN-190 and prazosin only slightly reduced body temp. In this species, however, NAN-190 showed marked antagonist activity against 8-OH-DPAT hypothermia. This was not due to .alpha.1-adrenoceptor antagonist activity as prazosin had no effect. In the rat, as in the mouse, RMY 7378 had a partial agonist profile, whereas WB 4101 behaved essentially as an agonist. These results suggest that NAN-190 is a pure antagonist of 8-OH-DPAT-induced hypothermia in rats and that RMY 7378 and WB 4101 are, resp., a partial agonist and an agonist in this test. The rat seems to be the better species for the study of 5-HT1A receptors using 8-OH-DPAT-induced hypothermia as it is less affected by .alpha.1-adrenoceptor antagonist activity and because the mouse model fails to demonstrate an interaction of NAN-190 with 5-HT1A receptors.
 IT 21102-95-4, RMY7378
 RL: BIOL (Biological study)
 (hydroxydipropylaminotetralin radn. in body temp. response to, serotonin receptor subtype and species in relation to)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 188 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:136473 CAPLUS
 DOCUMENT NUMBER: 114:136473
 TITLE: Agonist action at 5-HT1C receptors facilitates receptor-mediated spontaneous tail-flicks in the rat
 AUTHOR(S): Bervoets, Karin; Millan, Mark J.; Colpaert, Francis C.
 CORPORATE SOURCE: Neurobiol. Div., FONDAX, Putaux, 92800, Fr.
 SOURCE: Eur. J. Pharmacol. (1990), 191(2), 185-95
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In rats lightly restrained in plastic cylinders, s.c. administration of the selective, high-efficacy 5-HT1A receptor agonist 8-hydroxy-2-(dipropylamino)tetralin (8-OH-DPAT) induced spontaneous tail flicks. The putative 5-HT1B receptor agonist CGS 12066B, the mixed 5-HT1B/1C receptor agonists 1-[3-(trifluoromethyl)phenyl]piperazine (TFMPP) and 1-(3-chlorophenyl)piperazine (mCPP), the 5-HT1C/2 receptor agonist ((+,-)-1-(2,5-dimethoxy-4-iodophenyl)-2-aminopropane (DOI)), and the 5-HT1B/1C/2 receptor agonist quipazine did not elicit tail flicks when applied alone. However, TFMPP, mCPP, DOI, and quipazine, but not CGS 12066B, each potentiated the action of 8-OH-DPAT. Further, in the presence of TFMPP, mCPP, and DOI, the dose-receptor curve for the induction of tail flicks by 8-OH-DPAT was both steeper and shifted to the left. Tail flicks induced by another high-efficacy 5-HT1A receptor agonist, lisuride, were also enhanced by TFMPP, mCPP, and DOI. The 5-HT1A receptor partial agonists buspirone and (+,-)-flesinoxan evoked tail-flicks only in the presence of TFMPP, mCPP, or DOI. The mixed 5-HT1C/2 receptor antagonists ritanserin and ICI 169,369 did not modify the action of 8-OH-DPAT alone but abolished the potentiation of 8-OH-DPAT-induced tail flicks by DOI and TFMPP. Further, the selective 5-HT1A receptor antagonist RMY 7378 blocked tail flicks induced by both 8-OH-DPAT alone and 8-OH-DPAT plus DOI or TFMPP. A common property of these drugs potentiating 8-OH-DPAT-induced tail flicks is an agonist action at 5-HT1C receptors and the data indicate that it is this mechanism which underlies the facilitation of tail flicks.
 IT 21102-95-4, RMY 7378
 RL: BIOL (Biological study)
 (behavior induced by 5-HT1A and 5-HT1C receptor agonist inhibition)
 by)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

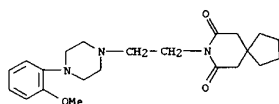
L14 ANSWER 189 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RL: BIOL (Biological study)
 (.alpha.2-adrenoceptor mediated submucosal plexus activity stimulation by UK 14304 inhibition by)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 189 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:36477 CAPLUS
 DOCUMENT NUMBER: 114:36477
 TITLE: Functional characterization of neuronal pre- and postsynaptic .alpha.2-adrenoceptor subtypes in guinea pig submucosal plexus
 AUTHOR(S): Shen, K. Z.; Barajas-Lopez, C.; Surprenant, A.
 CORPORATE SOURCE: Vollum Inst., Oregon Health Sci. Univ., Portland, OR, 97201, USA
 SOURCE: Br. J. Pharmacol. (1990), 101(4), 925-31
 CODEN: BJPCBM; ISSN: 0007-1188
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The .alpha.2-adrenoceptors on cell bodies of submucosal neurons, on presynaptic cholinergic nerve terminals innervating submucosal neurons, and on presynaptic sympathetic fibers innervating submucosal arterioles were characterized in functional studies by use of subtype selective ligands. Both membrane hyperpolarization and presynaptic inhibition of nicotinic excitatory synaptic potentials (e.p.s.ps) produced by UK 14304 were similarly antagonized by idazoxan, yohimbine, SKF 104078, WB 4101, and ARC 239. Antagonism was competitive and disocn. equil. consts. were the same for both effects. Vasoconstriction of submucosal arterioles in response to stimulation of the sympathetic nerves (20 Hz for 2 s) was inhibited by UK 14304 and clonidine; concns. producing half-max. responses were 6 and 10 nM, resp. Idazoxan, yohimbine, WB 4101, and SKF 104078 antagonized this action, with disocn. consts. similar to those for antagonism of the postsynaptic membrane hyperpolarization and presynaptic inhibition of nicotinic e.p.s.ps. Oxymetazoline was a partial agonist when membrane hyperpolarization or presynaptic inhibition of nicotinic e.p.s.ps were measured but a full agonist when presynaptic inhibition of sympathetically-mediated arteriolar vasoconstriction was measured. As an agonist, oxymetazoline produced half-max. responses at 80-120 nM; the disocn. const. for oxymetazoline as an antagonist was 130 nM. Neither prazosin nor chlorpromazine (up to 30 .mu.M) altered any of the 3 responses to .alpha.2-adrenoceptor agonists. Thus, .alpha.2-adrenoceptors present on submucosal neuronal cell bodies, on presynaptic cholinergic nerve terminals, and on presynaptic sympathetic nerve terminals are the .alpha.2A subtype. However, functional characterization of this subtype differs from that provided by ligand binding studies.
 IT 67339-62-2, ARC 239

L14 ANSWER 190 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1991:35858 CAPLUS
 DOCUMENT NUMBER: 114:35858
 TITLE: Behavioral effects of serotonin agonists and antagonists in the rat and marmoset
 AUTHOR(S): Elliott, P. J.; Walsh, D. M.; Close, S. P.; Higgins, G. A.; Hayes, A. G.
 CORPORATE SOURCE: Dep. Neuropharmacol., Glaxo Group Res. Ltd., Ware/Herts., SG12 0DP, UK
 SOURCE: Neuropharmacology (1990), 29(10), 949-56
 CODEN: NEPHEW; ISSN: 0028-3908
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The present study was conducted to investigate the effects of various 5-HT agonists and antagonists on motor behavior in rats and marmosets. Various motor-based responses were assessed after central or peripheral administration of 5-HT agents to rats and marmosets. Drugs acting as agonists at the 5-HT1A receptor (8-OHDPAT, gepirone, RMY-7378, NAN-190, PAPP (LY165163) and flesinoxan) and 5-HT2/1C receptors (DOI) were found to reverse neuroleptic-induced catalepsy in the rat, whereas 5-HT2/1C antagonists (mianserin, ritanserin and ICI-70,809) and the 5-HT1 antagonist ((+,-)-pindolol) increased catalepsy. Agonists acting at 5-HT3 receptors (phenylbiguanide and 2-methyl-5-HT) had no effect on catalepsy. The putative 5-HT1A antagonist, ((+,-)-pindolol, attenuated the reversal of catalepsy by 8-OHDPAT. Although both 8-OHDPAT and RMY-7378 were tested, only the latter was found to reduce apomorphine-induced stereotypy. Bilateral or unilateral infusions of 8-OHDPAT, RMY-7378 or pindolol into the substantia nigra of non-lesioned rats had no effect on spontaneous locomotor or rotational activity, resp. However, 8-OHDPAT and RMY-7378 were found to increase or decrease motor activity, after injection into the median or dorsal raphe nuclei, resp. Finally, 8-OHDPAT and RMY-7378 were found to be inactive against MPTP-induced bradykinesia in the marmoset. It is concluded that both 5-HT1A and 5-HT2/1C receptors are involved in the anti-cataleptic effects of 5-HT agents. The 5-HT1A receptors are probably situated within the raphe, whereas the location of the 5-HT2/1C receptors remains undetd.
 IT 21102-95-4, RMY 7378
 RL: BIOL (Biological study)
 (behavior response to, brain serotonergic receptors in)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-

L14 ANSWER 190 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

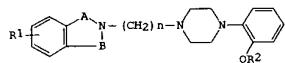


● 2 HCl

L14 ANSWER 191 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:12226 CAPLUS
DOCUMENT NUMBER: 114:12226
TITLE: Preparation of N,N'-disubstituted piperazines for treatment of dysuria
INVENTOR(S): Hachisu, Mitsugi; Yoshida, Seishi; Takahashi, Hiroko
PATENT ASSIGNEE(S): Ishii, Yuko; Tsuruoka, Takashi; Inoue, Shigeharu
SOURCE: Meiji Seika Kaisha, Ltd., Japan
Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKKXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

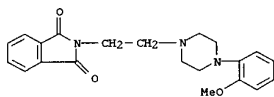
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 02184667 | A2 | 19900719 | JP 1989-5482 | 19890111 |

OTHER SOURCE(S): MARPAT 114:12226
GI

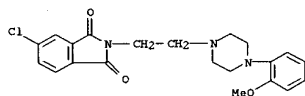


AB Pharmaceuticals for treatment of dysuria contain the title compds. I
(A = CH2, CO; B = CO, SO2; R1 = H, halo; R2 = Cl-3 alkyl; n = 2-4) or their pharmacol. acceptable salts as active ingredients. The treatment of 1-(2-methoxyphenyl)piperazine with 2-(2-bromoethyl)phthalimidine and Na2CO3 in DMF at room temp. for 16 h gave 73% 2-[4-(2-methoxyphenyl)piperazinoethyl]phthalimidine (II), which blocked .alpha.1-adrenaline receptor in aorta and urethra with pA2 of 8.1 and 8.2, resp., vs. 8.6 and 8.1, for the control contg. prazosin, resp.
Tablets were formulated contg. II 10.0, lactose 86.8, corn starch 37.0, poly(vinylpyrrolidone) 5.0, and Mg stearate 1.2 mg.
IT 99718-67-9P 130976-13-5P
RL: PREP (Preparation)
(prepn. of, for treatment of dysuria)
RN 99718-67-9 CAPLUS
CN 1H-isoindole-1,3(2H)-dione, 5-chloro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

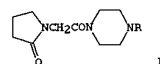
L14 ANSWER 191 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 130976-13-5 CAPLUS
CN 1H-isoindole-1,3(2H)-dione, 5-chloro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

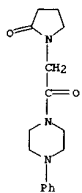


L14 ANSWER 192 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:6443 CAPLUS
DOCUMENT NUMBER: 114:6443
TITLE: Potential nootropic agents: synthesis of a series of
(2-oxo-1-pyrrolidinyl)acetic acid piperazides
AUTHOR(S): Valenta, Vladimir; Sindelar, Karel; Holubek, Jiri; Ryska, Miroslav; Krejci, Ivan; Dlabac, Antonin; Protiva, Miroslav
CORPORATE SOURCE: Res. Inst. Pharm. Biochem., Prague, 130 60, Czech.
SOURCE: Collect. Czech. Chem. Commun. (1990), 55(6), 1613-29
CODEN: CCCCAK; ISSN: 0010-0765
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 114:6443
GI

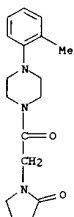


AB The title compds., e.g., I (R = Me, CH2CH2OMe, CH2Ph, CO2Et, Ph, substituted Ph) were prepd. by heating Et (2-oxo-1-pyrrolidinyl)acetate with a series of N-monosubstituted piperazines. The propionamides' e.g., I (CH2CH2CONH2), were obtained by reactions of the acid chlorides with 3-(1-piperazinyl)propionamide. I (R = Me, CH2CH2OMe) proved more active than piracetam by their anti-amnesic effects in rats, by antagonizing the brain-damaging effects of cycloheximide in infantile rats, and by their potentiation of the effects of anticonvulsant agents.
IT 131027-95-7P 131027-96-8P 131027-97-9P
131027-98-0P 131027-99-1P 131028-00-7P
131028-01-8P 131028-02-9P 131028-23-4P
131028-24-5P 131028-25-6P 131028-26-7P
131028-27-8P 131028-28-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 131027-95-7 CAPLUS
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)

L14 ANSWER 192 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

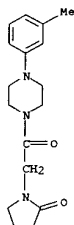


RN 131027-96-8 CAPLUS
CN Piperazine, 1-(2-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)
(CA INDEX NAME)

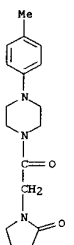


RN 131027-97-9 CAPLUS
CN Piperazine, 1-(3-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)
(CA INDEX NAME)

L14 ANSWER 192 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

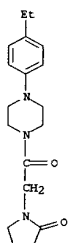


RN 131027-98-0 CAPLUS
CN Piperazine, 1-(4-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)
(CA INDEX NAME)

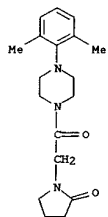


RN 131027-99-1 CAPLUS
CN Piperazine, 1-(4-ethylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)
(CA INDEX NAME)

L14 ANSWER 192 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

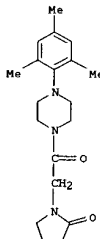


RN 131028-00-7 CAPLUS
CN Piperazine, 1-(2,6-dimethylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)
(CA INDEX NAME)

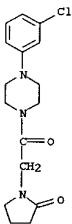


RN 131028-01-8 CAPLUS
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-(2,4,6-trimethylphenyl)- (9CI)
(CA INDEX NAME)

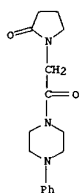
L14 ANSWER 192 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 131028-02-9 CAPLUS
CN Piperazine, 1-(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]- (9CI)
(CA INDEX NAME)

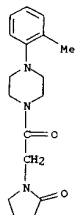


RN 131028-23-4 CAPLUS
CN Piperazine, 1-[(2-oxo-1-pyrrolidinyl)acetyl]-4-phenyl-, monohydrochloride (9CI)
(CA INDEX NAME)



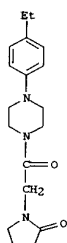
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RN 131028-24-5 CAPLUS
 CN Piperazine, 1-[(2-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)



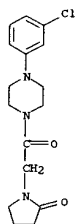
● HCl

RN 131028-25-6 CAPLUS
 CN Piperazine, 1-[(3-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

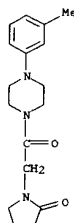


● HCl

RN 131028-28-9 CAPLUS
 CN Piperazine, 1-[(3-chlorophenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

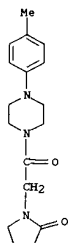


● HCl



● HCl

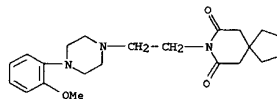
RN 131028-26-7 CAPLUS
 CN Piperazine, 1-[(4-methylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 131028-27-8 CAPLUS
 CN Piperazine, 1-[(4-ethylphenyl)-4-[(2-oxo-1-pyrrolidinyl)acetyl]-, monohydrochloride (9CI) (CA INDEX NAME)

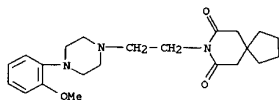
L14 ANSWER 193 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1990:604753 CAPLUS
 DOCUMENT NUMBER: 113:204753
 TITLE: 5-HT1A agonist effects on punished responding of squirrel monkeys
 AUTHOR(S): Gleeson, S. J. Barrett, J. E.
 CORPORATE SOURCE: Dep. Psychiatry, Uniformed Serv. Univ. Health Sci., Bethesda, MD, 20889-4799, USA
 SOURCE: Pharmacol., Biochem. Behav. (1990), 37(2), 335-7
 CODEN: PBEHAU; ISSN: 0091-3057
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Buspirone and other drugs that act as 5-HT1A agonists appear to be effective anxiolytics in humans, yet their anticonflict effects, though robust in pigeons, are equivocal in rodents. In the present study the effects of the benzodiazepine midazolam and a series of 5-HT1A agonists were examd. on punished responding of squirrel monkeys. Lever presses were reinforced according to a fixed-interval 3-min schedule; in addn., each 30th lever press was punished. Midazolam produced large increases in response rates, whereas none of the 5-HT1A compds. produced any increases in responding. Most of these drugs decreased response rates at the higher doses examd. Although the reasons for the discrepancy between species in the anticonflict effects of serotonergic anxiolytics cannot be specified, the different anatomical distribution of 5-HT1A binding sites across species may suggest a different functional role for this receptor.
 IT 21102-95-4, BMY 7378
 RL: BIOL (Biological study)
 (punished behavior response to, in squirrel monkeys)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

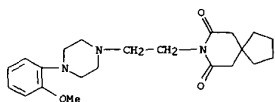
L14 ANSWER 194 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1990:471240 CAPLUS
 DOCUMENT NUMBER: 113:71240
 TITLE: RMY 7378: partial agonist at spinal cord 5-HT1A receptors
 AUTHOR(S): Zemian, Frank P.; Zieleniewski-Murphy, Anne; Murphy, R. Maureen; Behbehani, Michael M.
 CORPORATE SOURCE: Coll. Med., Univ. Cincinnati, Cincinnati, OH, 45267-0559, USA
 SOURCE: Neurochem. Int. (1990), 16(4), 515-22
 CODEN: NEUVIDS; ISSN: 0197-0186
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Recent data indicate that RMY 7378 demonstrates high affinity, selectivity and low intrinsic activity at hippocampal 5-HT1A receptors, suggesting that RMY 7378 may represent the first selective 5-HT1A functional antagonist. The present study examd. the agonist and antagonist properties of RMY 7378 at spinal cord 5-HT1A receptors. In electrophysiol. studies, iontophoretic administration of either the 5-HT1A agonist 8-OH-DPAT (43.8 nA) or RMY 7378 (46.3 nA) significantly inhibited the firing rate of wide-dynamic-range dorsal horn units indicating that RMY 7378 demonstrates significant intrinsic activity at spinal cord 5-HT1A receptors. Concomitant RMY 7378 and 8-OH-DPAT administration identified no RMY 7378 ejection current (20-100 nA) which antagonized the 8-OH-DPAT induced inhibition of dorsal horn unit activity. In behavioral studies in the spinal rat, 8-OH-DPAT increased the animals' sensitivity to noxious levels of mech. stimulation (ED50 = 269 nmol/kg) as did RMY 7378 (ED50 = 295 nmol/kg) with no statistically significant differences in the maximal response (Ymax) obsd. Concomitant RMY 7378 and 8-OH-DPAT administration identified no RMY 7378 dose (10-1100 nmol/kg) which blocked the hyperalgesic effect of 8-OH-DPAT, rather, each drug produced similar effects which were additive. Further, the 5-HT1A-agonist effects of RMY 7378 were blocked by the 5-HT1A antagonist spiperone. Therefore, both the electrophysiol. and reflex data indicate that RMY 7378 possesses intrinsic activity at spinal cord 5-HT1A receptors, and like 8-OH-DPAT is a partial agonist at these receptors. Differences in RMY 7378 intrinsic activity at spinal cord as opposed to hippocampal 5-HT1A receptors are discussed in terms of regional differences in G-proteins coupled to 5-HT1A receptors in

L14 ANSWER 194 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 IT these two CNS regions.
 21102-95-4, RMY 7378
 RL: BIOL (Biological study)
 (as serotonergic 51A receptor partial antagonist, in spinal cord)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



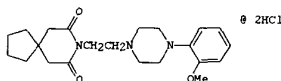
●2 HCl

L14 ANSWER 195 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1990:471154 CAPLUS
 DOCUMENT NUMBER: 113:71154
 TITLE: RU 24969-induced emesis in the cat: 5-HT1 sites other than 5-HT1A, 5-HT1B or 5-HT1C implicated
 AUTHOR(S): Lucot, James B.
 CORPORATE SOURCE: Dep. Pharmacol., Wright State Univ., Dayton, OH, 45435, USA
 SOURCE: Eur. J. Pharmacol. (1990), 180(2-3), 193-9
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB RU 24969 was administered s.c. to cats and found to elicit with a maximally ED of 1.0 mg/kg. 5-Methoxytryptamine was found to have lower efficacy and to produce a higher incidence of non-specific effects while trifluoromethylphenylpiperazine was devoid of emetic effects. The emesis elicited by 1.0 mg/kg of RU 24969 was not altered by pretreatment with phentolamine, haloperidol, yohimbine or (-)-propranolol, indicating that catecholamines played no role in this response. The emesis was prevented by metergoline and methylsergide but not by ketanserin, cyproheptadine, mesulergine, ICS 205,930, methiothepin, trimethobenzamide or RMY 7378. An indirect argument is presented that implicates a role for 5-HT1D sites. This conclusion must remain tentative until drugs selective for this site are synthesized and tested. The emesis was also prevented by 8-hydroxy-2-(di-n-propylamine)tetralin, confirming that this drug has a general antiemetic effect in cats.
 IT 21102-95-4, RMY 7378
 RL: BIOL (Biological study)
 (RU 24969-induced emesis response to, serotonin receptor sites in relation to)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

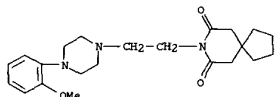
L14 ANSWER 196 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1990:191749 CAPLUS
 DOCUMENT NUMBER: 112:191749
 TITLE: Further investigation of the in vivo pharmacological properties of the putative 5-HT1A antagonist, RMY 7378
 AUTHOR(S): Sharp, Trevor; Backus, Lisa I.; Hjorth, Stephan; Bramwell, Steven R.; Grahame-Smith, David G.
 CORPORATE SOURCE: Dep. Clin. Pharmacol., Radcliffe Infirmary, Oxford, OX2
 SOURCE: GHE, UK
 Eur. J. Pharmacol. (1990), 176(3), 331-40
 CODEN: EJPJAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



I

AB The present study examined the action of the putative 5-HT1A antagonist, RMY 7378 (1) on central pre- and postsynaptic 5-HT1A function in the rat in vivo. Unlike the direct acting 5-HT1A agonist 8-hydroxy-2-(dipropylamino)tetralin (8-OH-DPAT), RMY 7378 (0.25-5 mg/kg s.c.) did not induce the full postsynaptically mediated 5-HT behavioral syndrome (forepaw treading, head weaving, flat body posture, hindlimb abduction). Indeed, the maximal 5-HT behavioral syndrome scores for RMY 7378 were about 10% of those for 8-OH-DPAT. Following pretreatment, however, RMY 7378 concn.-dependently (0.25-5 mg/kg s.c.) reduced to undetectable levels forepaw treading and head weaving induced by 8-OH-DPAT (0.75 mg/kg s.c.). RMY 7378 also inhibited stereotypy and locomotor activity induced by 0.5 mg/kg apomorphine at 5 mg/kg. In contrast to its apparent 5-HT1A antagonist properties in the behavioral expts., RMY 7378 caused a marked and concn.-dependent (0.01-1.0 mg/kg s.c.) decrease of 5-HT release in ventral hippocampus of the anesthetized rats as detected by brain microdialysis. This effect of RMY 7378 had a similar onset and duration of action but with slightly reduced efficacy compared to that previously described for 8-OH-DPAT. As with 8-OH-DPAT, the inhibitory effect of RMY

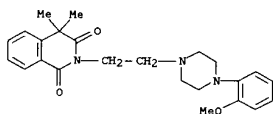
L14 ANSWER 196 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 7378 on 5-HT release was attenuated by pretreatment with the 5-HT1 receptor/.beta.-adrenoceptor antagonist pindolol (8 mg/kg s.c.) but not its counterpart propranolol (20 mg/kg s.c.). Pretreatment with a combination of the .beta.1- and .beta.2-adrenoceptor antagonists metoprolol (4 mg/kg s.c.) and ICI 118551 (4 mg/kg s.c.), resp., did not alter the 5-HT response to RMY 7378. RMY 7378 is a mixed agonist/antagonist at central 5-HT1A receptors.
 IT 21102-95-4, RMY 7378
 RL: BIOL (Biological study)
 (serotonergic SIA receptors of brain response to, mixed agonist-antagonist activity in relation to)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (HCl) (CA INDEX NAME)



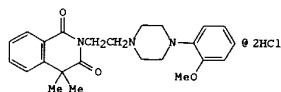
● 2 HCl

L14 ANSWER 197 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1990:152352 CAPLUS
 DOCUMENT NUMBER: 112:152352
 TITLE: Subtypes of .alpha.1-adrenoceptors in hippocampus of pigs, guinea pigs, calves and humans: regional differences
 AUTHOR(S): Hoyer, Daniel; Jones, C. Richard; Ford, William; Palacios, Jose M.
 CORPORATE SOURCE: Preclin. Res., Sandoz Ltd., Basel, CH-4002, Switz.
 SOURCE: Eur. J. Pharmacol., Mol. Pharmacol. Sect. (1990), 188(1), 9-16
 CODEN: EJPJET; ISSN: 0922-4106
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Radioligand binding studies were performed with membranes of guinea-pig, pig, calf, and human hippocampus using [125I]-labeled BE 2254 (also known as [125I]-labeled HEAT as the radioligand. [125I]-labeled BE 2254 bound with similar high affinity to saturable populations of recognition sites in all 4 membrane preps. Competition curves obtained with a variety of ligands (e.g., WB 4101, benoxathian, 5-methyl-urapidil) were biphasic and the profiles of the high- and low-affinity components of [125I]-labeled BE 2254 binding were similar in all four membrane preps. The data suggest that [125I]-labeled BE 2254 labels 2 subtypes of .alpha.1-adrenoceptors in the hippocampus of these species. [3H]WB 4101 was used to label .alpha.1A recognition sites in pig hippocampus membranes. [3H]WB 4101 recognized with high affinity an apparently homogeneous class of sites, as suggested by monophasic satn. and competition expts. The rank order of affinity of the compds. for the high-affinity component of [125I]-labeled BE 2254 binding was similar to the rank order of affinity of these drugs for [3H]WB 4101 sites. The pharmacol. profile of the low-affinity component of [125I]-labeled BE 2254 binding was similar to that described recently for the .alpha.1B-adrenoceptor cloned from DDT1 cells. In autoradiog. studies with human hippocampal slices, CEC (chloroethylclonidine), an alkylating agent described to show selectivity for .alpha.1B-adrenoceptors, displaced preferentially [125I]-labeled BE 2254 binding from the mol. layer of the dentate gyrus. In contrast, WB 4101 and .alpha.1A-adrenoceptor-selective ligand, displaced preferentially [125I]-labeled BE 2254 binding in the hilus and the CA3 region. The data show that 2 subtypes of .alpha.1-adrenergic recognition sites can be identified in the hippocampus. In the human hippocampus, .alpha.1A sites

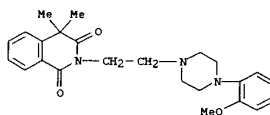
L14 ANSWER 197 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 are predominant in the hilus and the CA3 region, whereas .alpha.1B
 sites are predominant in the mol. layer of the dentate gyrus. These
 subtypes show a similar pharmacol. profile in man, pig, calf and guinea-pig,
 and may have a different functional role in these two areas of the
 hippocampus.
 IT 67339-62-2, ARC 239
 RL: BIOL (Biological study)
 (.alpha.1 adrenoceptor subtypes affinity for, of hippocampus of
 human and lab. animal)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 198 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1990:62442 CAPLUS
 DOCUMENT NUMBER: 112:62442
 TITLE: Infrared spectroscopy study of interactions
 affecting
 AUTHOR(S): tablet disintegration and drug release rate
 Casahoursat, L.; Pham Van Huong; Larrouture, D.;
 Heraud, P.; Etienne, A.
 CORPORATE SOURCE: Inst. Pharm. Ind., Bordeaux, 33000, Fr.
 SOURCE: Pharm. Acta Helv. (1989), 64(8), 225-30
 CODEN: PAHEAA; ISSN: 0031-6865
 DOCUMENT TYPE: Journal
 LANGUAGE: French
 GI



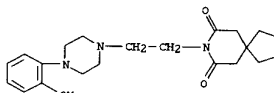
AB IR spectroscopy studies showed that the interaction between the drug
 (e.g., ARC.2HCL) (I) and excipients necessary for tablet formulations
 affected the drug release rate. The interaction was higher at higher
 compression pressures.
 IT 55974-42-0
 RL: PRP (Properties)
 (interaction of, with excipients, IR spectroscopy study of)
 RN 55974-42-0 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX
 NAME)



● 2 HCl

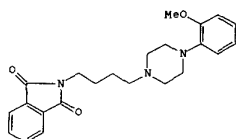
L14 ANSWER 199 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1989:587453 CAPLUS
 DOCUMENT NUMBER: 111:187459
 TITLE: Behavioral studies with anxiolytic drugs. VI.
 Effects on punished responding of drugs
 interacting
 with serotonin receptor subtypes
 AUTHOR(S): Gleason, S.; Ahlers, S. T.; Mansbach, R. S.;
 Foust, J.
 CORPORATE SOURCE: M.; Barrett, J. E.
 Dep. Psychiatry, Uniformed Serv. Univ. Health
 Sci.,
 SOURCE: Bethesda, MD, 20814-4799, USA
 J. Pharmacol. Exp. Ther. (1989), 250(3), 809-17
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The effects of drugs that bind selectively to different 5-HT receptor
 subtypes were assessed in pigeons. Keypecking was maintained by a
 multiple fixed-ratio schedule of reinforcement in which responding
 also was punished during one component. The greatest increases in
 punished responding were produced by the buspirone analogs RMY 7378 and
 ipsaspirone, which act at the 5-HT1A receptor. RU 24969, with high affinity for
 both 5-HT1A and 5-HT1B receptors, and 1-(2-methoxyphenyl)piperazine, a
 5-HT1 compd., increased punished responding to a lesser extent, as did the
 5-HT2 antagonists ketanserin and ritanserin. The 5-HT3 antagonists GR
 38032F, ICS 205930, and MDL 72222 showed little systematic effect, and the
 mixed 5-HT1B/5-HT1C compd. 1-(3-chlorophenyl)piperazine decreased punished
 responding. Levels of neurotransmitter metabolites in cerebrospinal
 fluid were assessed across a wide dose range of representative drugs used
 in the behavioral studies. Levels of the 5-HT metabolite 5-HIAA were
 decreased by RMY 7378 and ipsaspirone, were not changed by ritanserin, and were
 increased at one dose by MDL 72222. Thus, decreased 5-HT
 neurotransmission is involved in the effects of novel
 nonbenzodiazepine anxiolytics such as buspirone. The effects of these drugs on other
 neurotransmitter systems do not play a significant role in their
 anxiolytic actions.
 IT 21102-95-4, RMY 7378
 RL: PRP (Properties)
 (behavioral anxiolytic effect of, serotonin receptor subtypes in,
 cerebrospinal fluid monoamine metabolites response to)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 199 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● 2 HCl

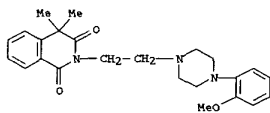
L14 ANSWER 200 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1989:205083 CAPLUS
 DOCUMENT NUMBER: 110:205083
 TITLE: Stimulus properties of Arylpiperazines:
 NAN-190, a potential 5-HT1A serotonin antagonist
 AUTHOR(S): Glennon, R. A.; Naiman, M. A.; Pierson, M. E.;
 Titeler, M.; Lyon, R. A.; Herndon, J. L.;
 Misenheimer, B.
 CORPORATE SOURCE: Med. Coll. Virginia, Virginia Commonw. Univ.,
 Richmond, VA, 23298-0581, USA
 SOURCE: Drug Dev. Res. (1989), 16(2-3-4), 335-43
 CODEN: DDREDK; ISSN: 0272-4391
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



1

AB Arylpiperazines bind both at 5-HT1A and 5-HT1B serotonin receptors.
 In an attempt to design novel 5-HT1A agonists and antagonists based on the
 arylpiperazine nucleus, the stimulus properties of a series of such
 agents were studied in rats trained to discriminate 0.5 mg/kg of the 5-HT1B
 activity. The agents were modified to eliminate those features and
 to incorporate structural features important for the 5-HT1A activity.
 The resulting agents displayed high affinity for 5-HT1A sites. NAN-190 1
 neither mimicked nor antagonized the TMPP stimulus, but was capable
 of antagonizing the stimulus produced by the 5-HT1A agonist
 8-hydroxy-2-(dipropylamino)tetralin (0.2 mg/kg). NAN-190 may be a
 potential 5-HT1A antagonist.
 IT 21102-95-4, BMY 7378
 RL: BIOL (Biological study)
 (serotonin receptors interaction with, structure in relation to)
 RN 21102-95-4 CAPLUS
 CN 8-Azasp[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

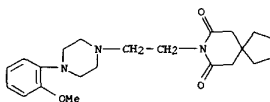
L14 ANSWER 201 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1989:101584 CAPLUS
 DOCUMENT NUMBER: 110:101584
 TITLE: Demonstration by infrared spectroscopy of the
 interactions affecting disintegration time of
 tablets and drug release rate
 AUTHOR(S): Casanourat, L.; Pham V. Huong; Larrouette, D.;
 Heraud, P.; Etienne, A.
 CORPORATE SOURCE: Inst. Pharm. Ind., Bordeaux, 33000, Fr.
 SOURCE: Bull. Tech./Gattefosse Rep. (1987), 80, 33-40
 CODEN: BTGRDQ
 DOCUMENT TYPE: Journal
 LANGUAGE: French
 AB IR spectroscopy showed that the interaction between a drug [e.g. AR-C
 239-2HCl (I)] and various excipients required for tablet formulation
 affected the disintegration time of tablets, but not the drug
 dissoln. rate. The excipients used were lactose, corn starch, gelatin, Mg
 stearate and poly(vinylpyrrolidone). The dissoln. rate of AR-C-HCl was not
 affected by the compression force, while that of I decreased with an
 increase in the compression force. The IR method was superior to
 the DSC method currently used.
 IT 55974-42-0 86891-00-1
 RL: BIOL (Biological study)
 (tablets, disintegration of and drug release rate from, excipient
 interactions effect on, IR spectroscopy study of)
 RN 55974-42-0 CAPLUS
 CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX
 NAME)



●2 HCl

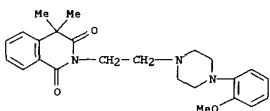
RN 86891-00-1 CAPLUS
 CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4,4-dimethyl-, monohydrochloride (9CI) (CA INDEX
 NAME)

L14 ANSWER 200 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



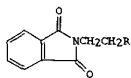
●2 HCl

L14 ANSWER 201 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



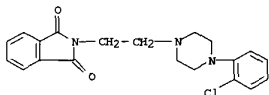
● HCl

L14 ANSWER 202 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1989:18097 CAPLUS
 DOCUMENT NUMBER: 110:18097
 TITLE: Antipsychotic properties of new
 N-(4-substituted-1-piperazinylethyl)- and N-(4-substituted-1-piperidinylethyl)-phthalimides
 AUTHOR(S): Al-Rashood, Khalid A.; Mustafa, Ali A.; Alhaider, Abdulqader; Ginawi, Omer T.; Madani, Abdul Azim
 E.:
 CORPORATE SOURCE: El-Obeid, Humeida A.
 Saudi Coll. Pharm., King Saud Univ., Riyadh, 11451,
 SOURCE: Arabia
 J. Pharm. Sci. (1988), 77(10), 898-901
 CODEN: JPMSAE; ISSN: 0022-3549
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



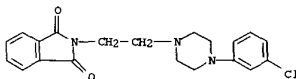
AB A series of N-(4-phenyl- and 4-pyridyl-1-piperazinylethyl)- and N-(4-phenyl-1-piperidinylethyl)-phthalimides I (R = 4-aryl-substituted piperazine and piperidine) were synthesized and tested for antipsychotic activity. All compds. suppressed the spontaneous motor activity and the apomorphine-induced climbing in mice and pergolide-induced locomotor activity in rats, demonstrating psychotropic properties equal to the that of sulpiride. Although the compds., like sulpiride, were less potent than haloperidol in blocking the locomotor activities, they caused no catalepsy, a major side effect following treatment with conventional antipsychotic agents. It is likely that the new compds. produce their neuroleptic activities through inhibition of limbic dopamine receptors.
 IT 75000-28-1P 75000-29-2P 75000-30-5P
 117992-67-3P 117992-68-4P 117992-69-5P
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prepn. and antipsychotic activity of)
 RN 75000-28-1 CAPLUS
 CN 1H-Indole-1,3(2H)-dione,
 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-

L14 ANSWER 202 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



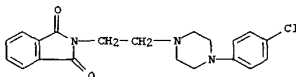
● HCl

RN 117992-68-4 CAPLUS
 CN 1H-Indole-1,3(2H)-dione,
 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
 , monohydrochloride (9CI) (CA INDEX NAME)



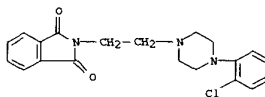
● HCl

RN 117992-69-5 CAPLUS
 CN 1H-Indole-1,3(2H)-dione,
 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
 , monohydrochloride (9CI) (CA INDEX NAME)

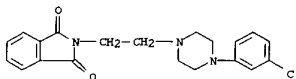


● HCl

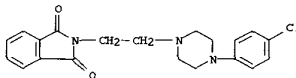
L14 ANSWER 202 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 75000-29-2 CAPLUS
 CN 1H-Indole-1,3(2H)-dione,
 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
 (9CI) (CA INDEX NAME)

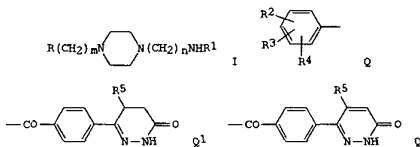


RN 75000-30-5 CAPLUS
 CN 1H-Indole-1,3(2H)-dione,
 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
 (9CI) (CA INDEX NAME)



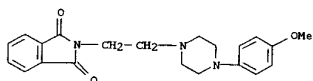
RN 117992-67-3 CAPLUS
 CN 1H-Indole-1,3(2H)-dione,
 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-
 , monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 203 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1988:590450 CAPLUS
 DOCUMENT NUMBER: 109:190450
 TITLE: Preparation of pyridazinone-containing piperazine derivatives and their salts as cardiotonics
 INVENTOR(S): Okujima, Hiromi; Narimatsu, Akihiro; Kobayashi, Makio;
 Furuya, Rikizo; Tsuda, Kunio; Kitada, Yoshi
 PATENT ASSIGNER(S): Mitsubishi Kasei Corp., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
 CODEN: JKOKAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:
 PATENT NO. KIND DATE APPLICATION NO. DATE
 JP 63154671 A2 19880627 JP 1986-300695 19861217
 OTHER SOURCE(S): MARPAT 109:190450
 GI

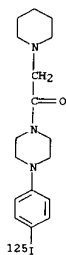


AB Title derivs. I (R = Q; R1 = Q1, Q2; R2 - R4 = H, C1-5 alkoxy, OH; R5 = H, C1-5 alkyl; two of R2 - R4 = OCH2O, OCH2CH2O; m = 0-4; n = 1-4) and their salts are prepd. as cardiotonics. A soln. of 1-(4-methoxyphenyl)piperazine and N-(2-bromoethyl)phthalimide in DMF was treated with Et3N at 80.degree. for 5 h and the product (yield 28%) was stirred with an aq. H2NNH2.H2O in EtOH at 70.degree. for 4 h to give 100 %
 I (R = C6H4OMe-4, R1 = H, m = 0, n = 2) (II).
 6-(4-Carboxyphenyl)-2,3,4,5-tetrahydropyridazin-3-one (0.75 g) was treated with ClCO2Et in DMF/THF contg. Et3N between -20 and -30.degree., the reaction mixt. was treated with a soln. of 0.81 g II at -20.degree. for 20 min, and then at room temp. for 2 h to give I (R = C6H4OMe-4, R1 = Q1, R5 = H, m = 0, n = 2) (III), which was treated with aq. HCl/EtOH to give 0.85 g III.HCl (IV).
 In guinea pig left atrium in vitro, IV at 10-5 or 3 .times. 10-5 g/mL

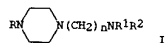
L14 ANSWER 203 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 increased cardiac contractility 42.1 or 58.0%, resp.
 IT 117046-73-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and redn. of)
 RN 117046-73-8 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-(4-(4-methoxyphenyl)-1-piperazinyl)ethyl]-
 (9CI) (CA INDEX NAME)



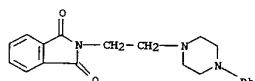
L14 ANSWER 204 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1988:586395 CAPLUS
 DOCUMENT NUMBER: 109:186395
 TITLE: The metabolic and kinetic aspects of
 1-(piperidinoacetyl)-4-(4-iodophenyl)piperazine: a
 potential brain imaging agent
 AUTHOR(S): Hariharan, Shankar
 CORPORATE SOURCE: Northeastern Univ., Boston, MA, USA
 SOURCE: (1987) 238 pp. Avail.: Univ. Microfilms Int.,
 Order
 No. DA8801974
 From: Diss. Abstr. Int. B 1988, 48(11), 3260
 DOCUMENT TYPE: Dissertation
 LANGUAGE: English
 AB Unavailable
 IT 117205-94-4, 1-(Piperidinoacetyl)-4-(4-[125I]iodophenyl)piperazine
 RL: BFR (Biological process); BIOL (Biological study); PROC (Process)
 (metab. of, brain imaging in relation to)
 RN 117205-94-4 CAPLUS
 CN Piperazine, 1-[4-(iodo-125I)phenyl]-4-(1-piperidinylacetyl)- (9CI)
 (CA INDEX NAME)



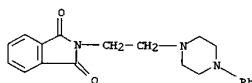
L14 ANSWER 205 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1988:528953 CAPLUS
 DOCUMENT NUMBER: 109:128953
 TITLE: Arylpiperazine derivatives as high-affinity
 5-HT1A
 serotonin ligands
 AUTHOR(S): Glennon, Richard A.; Naiman, Noreen A.; Lyon,
 Robert
 CORPORATE SOURCE: A.; Titeler, Milt
 Med. Coll. Virginia, Virginia Commonw. Univ.,
 Richmond, VA, 23298-0581, USA
 SOURCE: J. Med. Chem. (1988), 31(10), 1968-71
 CODEN: JMCNAR, ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 109:128953
 GI



AB A small series of 4-substituted 1-arylpiperazines I (R = Ph,
 2-MeOC6H4,
 1-naphthyl, 2-pyrimidinyl; NR1R2 = phthalimido, NH2, NHA, NHBz; n =
 2-5)
 was prepd. in an attempt to develop agents with high affinity for
 5-HT1A
 (5-hydroxytryptamine1A) serotonin binding sites. I (R = Ph,
 2-MeOC6H4,
 1-naphthyl; NR1R2 = phthalimido, NHBz; n = 4) displayed high
 affinities
 for these sites. One of these compds., I (R = 2-MeOC6H4, NR1R2 =
 phthalimido, n = 4), possessed a higher affinity than 5-HT and
 represents
 the highest affinity (K1 = 0.6 nM) agent yet reported for 5-HT1A
 sites.
 IT 75000-24-7P 115338-31-3P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and binding affinity of, for hydroxytryptamine receptor
 site)
 RN 75000-24-7 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-
 (9CI)
 (CA INDEX NAME)



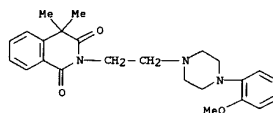
L14 ANSWER 205 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 115338-31-3 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-,
 monohydrochloride (9CI) (CA INDEX NAME)



● HCl

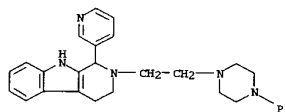
L14 ANSWER 206 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1988:417541 CAPLUS
 DOCUMENT NUMBER: 109:17541
 TITLE: Alpha-2A and alpha-2B adrenergic receptor
 subtypes: antagonist binding in tissues and cell lines
 containing only one subtype
 AUTHOR(S): Bylund, David B.; Ray-Pronger, Carla; Murphy, T.
 J.
 CORPORATE SOURCE: Sch. Med., Univ. Missouri, Columbia, MO, 65212,
 USA
 SOURCE: J. Pharmacol. Exp. Ther. (1988), 245(2), 600-7
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The affinities of 34 adrenergic antagonists for .alpha.2-adrenergic
 receptors were detd. from homogenate radioligand binding studies with
 [3H]yohimbine and [3H]rauwolscine. It has been suggested that
 .alpha.2-adrenergic receptors can be subdivided into .alpha.2A and
 .alpha.2B subtypes. Oxymetazoline is selective for .alpha.2A
 receptors, whereas prazosin is .alpha.2B selective. Five different tissues were
 used, each of which has only 1 of the 2 subtypes: human platelets
 (.alpha.2A), the HT29 cell line (.alpha.2A), human cerebral cortex
 (.alpha.2A), neonatal rat lung (.alpha.2B), and NG108-15 cell line
 (.alpha.2B). The drug affinities were highly correlated when
 .alpha.2A
 tissues were compared with .alpha.2A tissues (r = 0.97-0.98) or when
 the 2
 .alpha.2B tissues were compared (r = 0.99). By contrast, comparison
 of an
 .alpha.2A tissue with an .alpha.2B tissue resulted in poor
 correlations (r
 = 0.77 to -0.87). Three new subtype-selective drugs were identified
 among
 these drugs on the basis of at least a 10-fold greater affinity for 1
 subtype. All 3 were selective for the .alpha.2B subtype: ARC-239
 (100-fold selective), chlorpromazine (18-fold selective), and
 7-hydroxychlorpromazine (17-fold selective). These studies, by
 demonstrating distinct pharmacol. profiles for the 2
 .alpha.2-adrenergic
 receptor subtypes in several different tissues, further support the
 existence and definition of these subtypes. The identification of a
 cell
 line for each subtype should be useful in the further study of
 .alpha.2-adrenergic receptor subtypes.
 IT 67339-62-2, ARC 239
 RL: BIOL (Biological study)
 (as .alpha.2B adrenergic receptor ligand)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

L14 ANSWER 206 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

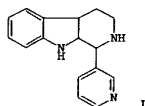


L14 ANSWER 207 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1987:568626 CAPLUS
 DOCUMENT NUMBER: 107:168626
 TITLE: Synthesis and pharmacological properties of some
 2-substituted
 1-(3-pyridyl)-1,2,3,4-tetrahydro-.beta.-
 carbolines
 AUTHOR(S): Misztal, Stanislaw; Boksa, Jan;
 Chojnacka-Wojcik, Ewa;
 Tatarczynska, Ewa; Lewandowska, Anna
 CORPORATE SOURCE: Inst. Pharmacol., Pol. Acad. Sci., Krakow,
 31-343,
 Pol.
 SOURCE: Pol. J. Pharmacol. Pharm. (1987), 39(1), 97-103
 CODEN: PJPPAA; ISSN: 0301-0244
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 107:168626
 GI

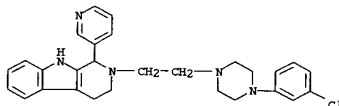
L14 ANSWER 207 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



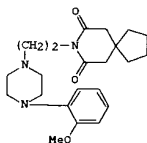
RN 110785-30-3 CAPLUS
 CN 1H-Pyrido[3,4-b]indole, 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
 2,3,4,9-tetrahydro-1-(3-pyridinyl)- (9CI) (CA INDEX NAME)



AB The title compds. I (R = COCH2NMe2, (CH2)2NMe2, COCH2piperidyl,
 (CH2)2piperidyl, etc.) were obtained by chloro- or bromoacetylation
 of
 1-(3-pyridyl)-1,2,3,4-tetrahydro-.beta.-carboline followed by
 reaction
 with the appropriate amine and LiAlH4 redn. Some of the compds.
 showed
 sedative properties in mice. None possessed neuroleptic,
 antidepressant,
 analgesic, or anticonvulsant properties.
 IT 110785-29-0P 110785-30-3P
 RL: ADV (Adverse effect, including toxicity); SPN (Synthetic
 preparation);
 BIOL (Biological study); PREP (Preparation)
 (prepn. and neuropharmacol. and toxicity of)
 RN 110785-29-0 CAPLUS
 CN 1H-Pyrido[3,4-b]indole, 2,3,4,9-tetrahydro-2-[2-(4-phenyl-1-
 piperazinyl)ethyl]-1-(3-pyridinyl)- (9CI) (CA INDEX NAME)

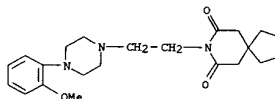


L14 ANSWER 208 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1987:489746 CAPLUS
 DOCUMENT NUMBER: 107:89746
 TITLE: RMY 7378, a buspirone analog with high affinity,
 selectivity and low intrinsic activity at the
 5-HT1A receptor in rat and guinea pig hippocampal
 membranes
 AUTHOR(S): Yocca, Frank D.; Hyslop, Deborah K.; Smith,
 David W.;
 CORPORATE SOURCE: Maayani, Saul
 Wallingford, Pharm. Res. Dev. Div., Bristol-Myers Co.,
 CT, 06492-7660, USA
 SOURCE: Eur. J. Pharmacol. (1987), 137(2-3), 293-4
 CODEN: EJPHAZ; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB The buspirone analog RMY7378 (1) had a high affinity and selectivity
 for 5-HT1A binding sites in rat and guinea pig hippocampal membrane
 preps.
 The drug also had low intrinsic activity.
 IT 21102-95-4
 RL: PROC (Process)
 (binding of, to serotonergic 5IA receptors of brain)
 RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-
 piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 208 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



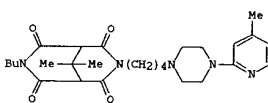
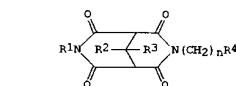
●2 HCl

L14 ANSWER 209 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1987:156511 CAPLUS
 DOCUMENT NUMBER: 106:156511
 TITLE: Preparation of
 3,7-diazabicyclo[3.3.1]nonane-2,4,6,8-
 tetrone derivatives as central nervous system
 agents
 INVENTOR(S): Schoen, Uwe; Kehrach, Wolfgang; Benson, Werner;
 Fuchs, Andreas; Ruhland, Michael
 PATENT ASSIGNEE(S): Kali-Chemie Pharma G.m.b.H., Fed. Rep. Ger.
 SOURCE: Ger. Offen., 11 pp.
 CODEN: GWXKXK
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

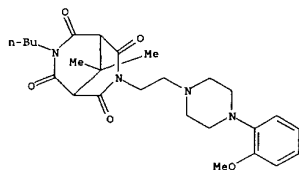
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|----------|
| DE 3529872 | A1 | 19870226 | DE 1985-3529872 | 19850821 |
| ES 556660 | A1 | 19871216 | ES 1986-556660 | 19860625 |
| FI 8603150 | A | 19870222 | FI 1986-3150 | 19860801 |
| FI 82048 | B | 19800928 | | |
| FI 82048 | C | 19910110 | | |
| EP 212551 | A2 | 19870304 | EP 1986-111145 | 19860812 |
| EP 212551 | A3 | 19880323 | | |
| EP 212551 | B1 | 19901024 | | |
| AT 57702 | BE, CH, DE, FR, GB, IT, LI, LU, NL, SE | 19901115 | AT 1986-111145 | 19860812 |
| HU 41788 | E | 19870528 | HU 1986-3603 | 19860818 |
| HU 194233 | B | 19880128 | | |
| ZA 8606243 | A | 19870429 | ZA 1986-6243 | 19860819 |
| DD 251555 | A5 | 19871118 | DD 1986-293732 | 19860819 |
| US 4771044 | A | 19880913 | US 1986-898043 | 19860819 |
| NO 8603346 | A | 19870223 | NO 1986-3346 | 19860820 |
| NO 164901 | B | 19900820 | | |
| NO 164901 | C | 19901128 | | |
| AU 8661619 | A1 | 19870226 | AU 1986-61619 | 19860820 |
| AU 589671 | B2 | 19891019 | | |
| DK 8603961 | A | 19870430 | DK 1986-3961 | 19860820 |
| DK 161648 | B | 19910729 | | |
| DK 161648 | C | 19920127 | | |
| IL 79785 | A1 | 19900712 | IL 1986-79785 | 19860820 |
| CA 1272196 | A1 | 19900731 | CA 1986-516366 | 19860820 |
| JP 62096489 | A2 | 19870502 | JP 1986-194120 | 19860821 |
| JP 07039416 | B4 | 19950501 | | |
| ES 557719 | A1 | 19880101 | ES 1987-557719 | 19870915 |
| JP 07267953 | A2 | 19951017 | JP 1994-265587 | 19941028 |
| JP 2525560 | B2 | 19960821 | | |
| PRIORITY APPLN. INFO.: | | | DE 1985-3529872 | 19850821 |
| | | | EP 1986-111145 | 19860812 |

GI

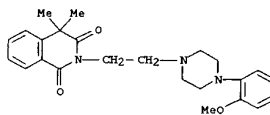
L14 ANSWER 209 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB The title compds. I [R1 = alkyl, alkenyl, cycloalkylalkyl,
 phenylalkyl;
 R2, R3 = alkyl, Ph; R2R3 = alkylene; R4 = nucleophilic leaving group,
 (un)substituted 1-piperazinyl; n = 2-10] were prepd. as central
 nervous system agents (no data). 3-Butyl-9,9-dimethyl-3,7-
 diazabicyclo[3.3.1]nonane-2,4,6,8-tetrone was alkylated with
 Br(CH2)4Br to
 give I (R1 = Bu, R2 = R3 = Me, R4 = Br, n = 4). This was condensed
 with
 1-(4-methyl-2-pyridinyl)piperazine to give diazabicyclononane II.
 Tablets, each contg. 20 mg II, were prepd. from II 20, cornstarch 30,
 lactose 55, polyvinylpyrrolidone 5, Mg stearate 2, and hydrogenated
 castor
 oil 1 part.
 IT 107736-97-0P
 RL: BAC (Biological activity or effector, except adverse); SPN
 (Synthetic
 preparation); THU (Therapeutic use); BIOL (Biological study); PREP
 (Preparation); USES (Uses)
 (prepn. of, as central nervous system agent)
 RN 107736-97-0 CAPLUS
 CN 3,7-Diazabicyclo[3.3.1]nonane-2,4,6,8-tetrone, 3-butyl-7-[2-[4-(2-
 methoxyphenyl)-1-piperazinyl]ethyl]-9,9-dimethyl- (9CI) (CA INDEX
 NAME)

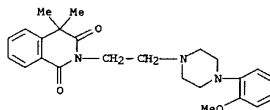


L14 ANSWER 210 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1987:149183 CAPLUS
 DOCUMENT NUMBER: 106:149183
 TITLE: The blood pressure effects of alpha-adrenoceptor antagonists injected in the medullary site of action
 of clonidine: the nucleus reticularis lateralis
 AUTHOR(S): Bousquet, Pascal; Feldman, Josiane
 CORPORATE SOURCE: Fac. Med., Univ. Louis Pasteur, Strasbourg, 67000, Fr.
 SOURCE: Life Sci. (1987), 40(11), 1045-52
 CODEN: LIFSAX; ISSN: 0024-3205
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A series of alpha-blocking drugs were administered to the nucleus reticularis lateralis (NRL) of the medulla oblongata, the main site for the hypotensive action of clonidine, in pentobarbital anesthetized cats. Drugs were injected through a needle which was stereotactically inserted. Prazosin [19216-56-9] (6 nmol) was hypertensive (MBP (mean blood pressure) = +25%), corynanthine [483-10-3] had no effect and AR-C239 [67339-62-2] (7 nmol), another alpha1-blocker, was hypotensive (MBP = -16%). The alpha2-blockers, yohimbine [146-48-5] and idazoxan [79944-58-4] were hypotensive. The blood pressure effects of alpha-blocking drugs directly microinjected in the nucleus reticularis lateralis cannot be simply related to their selectivity for a particular subtype of alpha-receptors.
 IT 67339-62-2, AR-C239
 RL: BIOL (Biological study)
 (blood pressure response to, after injection into nucleus reticularis lateralis, alpha-adrenergic receptor subtypes in)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 211 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1987:96671 CAPLUS
 DOCUMENT NUMBER: 106:96671
 TITLE: Alpha-1 adrenergic receptor binding and contraction of rat caudal artery
 AUTHOR(S): Abel, Peter W.; Minneman, Kenneth P.
 CORPORATE SOURCE: Sch. Med., Emory Univ., Atlanta, GA, 30322, USA
 SOURCE: J. Pharmacol. Exp. Ther. (1986), 239(3), 678-86
 CODEN: JPETAB; ISSN: 0022-3565
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Alpha-1 adrenergic receptors were examd. in rat caudal artery by using radioligand binding of 125I-labeled BE 2254 [40077-13-2] (125IBE) and in vitro contraction measurements. 125IBE bound rapidly and reversibly to a single class of high-affinity binding sites in membrane preps. of caudal artery. Scatchard anal. gave an equil. disocn. const. (KD) of 110 pM and a d. of binding sites of 115 fmol/mg of protein. Antagonists inhibited 125IBE binding and phenylephrine [59-42-7]-induced contractions competitively, with an order of potency of prazosin [19216-56-9] > ARC 239 [67339-62-2] > phentolamine [50-60-2] > yohimbine [146-48-5]. The pA2 (neg. log of antagonist concn. producing a half-max. effect) values for inhibition of phenylephrine-induced contraction correlated well with KD values for inhibition of specific 125IBE binding. A no. of other full and partial agonists also caused contraction of caudal arteries with an order of potency of epinephrine [51-43-4] > norepinephrine [51-41-2] > phenylephrine > methoxamine [390-28-3]. The order of potency of agonists and the potencies of antagonists suggests that the contractile responses of rat caudal artery were mediated by alpha-1 adrenergic receptors. The 50% effective concn. (EC50) values of partial agonists in causing contraction correlated well with their KD values for inhibition of specific 125IBE binding. However, the EC50 values for full agonists were 30-200-fold lower than their KD values. Treatment of caudal arteries in vitro with 0.1 .mu.M phenoxybenzamine for 10 min to inactivate alpha adrenergic receptors decreased both the potency of full agonists in causing contraction and the maximal contractile response. Functional equil. disocn. consts. calcd. from contraction expts. using phenoxybenzamine agreed well with KD's detd. from binding studies; however, phenoxybenzamine reduced 125IBE binding sites by 50%, whereas the theor. redn. in functional alpha adrenergic receptors averaged

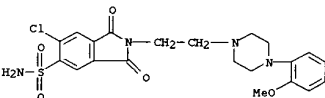
L14 ANSWER 211 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 96%. Apparently, 125IBE labels the alpha-1 adrenergic receptors mediating contraction of rat caudal artery. When receptor d. is reduced, the potencies of agonists in activating the receptors agree well with their potencies in binding to the receptors, suggesting that there is a pool of spare alpha-1 adrenergic receptors in this tissue.
 IT 67339-62-2, ARC 239
 RL: BIOL (Biological study)
 (caudal artery contraction by phenylephrine and .alpha.1-adrenergic ligand binding antagonism by)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



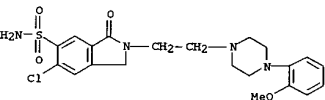
L14 ANSWER 212 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1986:424279 CAPLUS
 DOCUMENT NUMBER: 105:24279
 TITLE: 2-(1-Piperazinylalkyl)-1-oxo-1H-isoindoles
 INVENTOR(S): Dolak, Terence M.
 PATENT ASSIGNEE(S): Bristol-Myers Co., USA
 SOURCE: Ger. Offen., 84 pp.
 CODEN: GWXXEX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|--------------------|----------|
| DE 3524635 | A1 | 19860123 | DE 1985-3524635 | 19850710 |
| US 4585773 | A | 19860429 | US 1984-629649 | 19840711 |
| CA 1255311 | A1 | 19890606 | CA 1985-485831 | 19850628 |
| ZA 8505092 | A | 19860226 | ZA 1985-5092 | 19850705 |
| FI 8502694 | A | 19860112 | FI 1985-2694 | 19850708 |
| FI 79837 | B | 19891130 | | |
| FI 79837 | C | 19900312 | | |
| SE 8503415 | A | 19860112 | SE 1985-3415 | 19850709 |
| SE 457449 | B | 19881227 | | |
| SE 457449 | C | 19890420 | | |
| ES 545003 | A1 | 19870501 | ES 1985-545003 | 19850709 |
| BE 902847 | A1 | 19860110 | BE 1985-215319 | 19850710 |
| DK 8503150 | A | 19860112 | DK 1985-3150 | 19850710 |
| DK 163057 | B | 19920113 | | |
| DK 163057 | C | 19920609 | | |
| NO 8502779 | A | 19860113 | NO 1985-2779 | 19850710 |
| NO 163775 | B | 19900409 | | |
| AU 8544764 | A1 | 19860116 | AU 1985-44764 | 19850710 |
| AU 584104 | B2 | 19890518 | | |
| FR 2567519 | A1 | 19860117 | FR 1985-10587 | 19850710 |
| FR 2567519 | B1 | 19900413 | | |
| GB 2161807 | A1 | 19860122 | GB 1985-17418 | 19850710 |
| GB 2161807 | B2 | 19871209 | | |
| HU 39177 | A2 | 19860828 | HU 1985-2669 | 19850710 |
| HU 195213 | B | 19880428 | | |
| NL 8501998 | A | 19860203 | NL 1985-1998 | 19850711 |
| JP 61036260 | A2 | 19860220 | JP 1985-153333 | 19850711 |
| JP 04000066 | B4 | 19920106 | | |
| AT 8502062 | A | 19870815 | AT 1985-2062 | 19850711 |
| AT 385270 | B | 19880310 | | |
| CH 664964 | A | 19880415 | CH 1985-3016 | 19850711 |
| JP 61178964 | A2 | 19860811 | JP 1985-271277 | 19851202 |
| ES 552108 | A1 | 19870801 | ES 1986-552108 | 19860217 |
| NO 8703462 | A | 19860113 | NO 1987-3462 | 19870817 |
| DK 9100066 | A | 19910114 | DK 1991-66 | 19910114 |
| PRIORITY APPLN. INFO.: | | | US 1984-629649 | 19840711 |
| | | | NO 1985-2779 | 19850710 |
| OTHER SOURCE(S): | | | CASREACT 105:24279 | |
| GI | | | | |

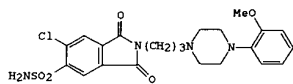
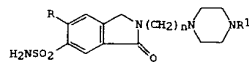
L14 ANSWER 212 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



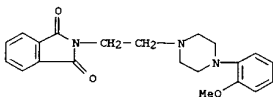
IT 102391-72-0P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as antihypertensive and diuretic)
 RN 102391-72-0 CAPLUS
 CN 1H-isoindole-5-sulfonamide,
 6-chloro-2,3-dihydro-2-[2-(4-(2-methoxyphenyl)-
 1-piperazinyl)ethyl]-3-oxo- (9CI) (CA INDEX NAME)



L14 ANSWER 212 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



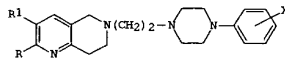
AB The title compds. [I; R = halo, F3C; R1 = (un)substituted Ph, PhCH2, Bz, 2-pyridyl; n = 2-5] were prepd. as antihypertensives and diuretics. Thus, 1-(2-methoxyphenyl)piperazine was quant. condensed with N-(3-bromopropyl)phthalimide and the product deprotected with N2H4 to give 95% 1-(3-aminopropyl)-4-(2-methoxyphenyl)piperazine. This was condensed with 4-chloro-5-sulfamoylphthalimide to give 61% (piperazinylpropyl)phthalimide II which was selectively reduced with Zn in HOAc to give 77% I (R = Cl, R1 = 2-MeOC6H4) (III). In rats 30 mg III/kg reduced blood pressure 84 mmHg.
 IT 99718-67-9P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and hydrazinolysis of)
 RN 99718-67-9 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione,
 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-
 (9CI) (CA INDEX NAME)



IT 102391-88-8P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and redn. of)
 RN 102391-88-8 CAPLUS
 CN 1H-isoindole-5-sulfonamide,
 6-chloro-2,3-dihydro-2-[2-(4-(2-methoxyphenyl)-
 1-piperazinyl)ethyl]-1,3-dioxo- (9CI) (CA INDEX NAME)

L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1986:141729 CAPLUS
 DOCUMENT NUMBER: 104:141729
 TITLE: Antivertigo agents. V. Quantitative structure-activity relationships of 6-[2-(4-aryl-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-1,6-naphthyridines
 AUTHOR(S): Shiozawa, Akira; Kogo, Yoshiya; Ichikawa, Yuhichiro;
 Shuji; Komuro, Chikara; Ishikawa, Michio; Kurashige, Miyazaki, Hiroshi; Yamanaka, Hiroshi; Sakamoto, Takao
 CORPORATE SOURCE: Res. Lab., Nippon Kayaku Co., Tokyo, 115, Japan
 SOURCE: Chem. Pharm. Bull. (1985), 33(12), 5332-40
 CODEN: CPBTAL; ISSN: 0009-2363
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI

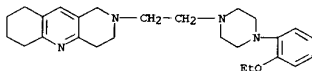


AB The quant. structure-activity relationships (QSAR) between the mol. structures and antivertigo activities of 6-[2-(4-aryl-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-1,6-naphthyridines I (R1R2 = (CH2)4; R1 = R2 = H; X = H, F, Cl, Me, NMe2, OMe, OEt, SMe, etc.) were investigated. The effects of the ortho-, meta-, and para-substituents on the Ph ring of the arylpiperazine moiety were examd. by means of regression anal. using various physicochem. parameters related to these substituents. The results showed that only the parameters concerning the ortho-substituent were statistically significant. Namely, the relative activity depended on both Fortho (Swain-Lupton field effect const. of the ortho-substituent) and I (indicator variable for the presence of an o-alkoxy group and an o-dimethylamino group). Thus, regression anal. for only the ortho-substituted compds. was examd. and afforded a result similar to that described above. Further, the net at. charge calcd. by the MO method besides free energy-related substituent parameters was used as electronic parameters of the ortho-substituents on the Ph ring for this QSAR anal. For the ortho-substituted compds. alone, the potency correlated well with

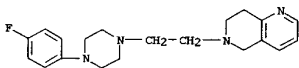
L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
the net at. charge on the first atom of the ortho-substituent (Qortho), while the correlation for all the compds. (ortho-, meta-, and para-substituents) was slightly lower than that for the ortho-substituted compds. alone. It was found that increase in the neg. net at. charge on the first atom of the ortho-position increased the relative activity. The correlation between Qortho, and Portho and I was examd. and the role of I is discussed in connection with H bond-forming ability. The interaction between the arylpiperazine moiety in the compd. and a putative receptor is discussed based on the QSAR anal.

IT 83081-77-0 83082-17-1 83082-23-9
83082-27-3 83082-29-8 83082-65-9
83100-19-0 83100-22-8 83100-24-7
83100-35-0 95355-89-8 95355-91-2
95355-93-4 95355-95-6 95355-97-8
95355-99-0 95356-01-7 95356-06-2
95356-07-3 95356-08-4 95356-09-5
95356-10-8 95356-11-9 95356-12-0
95356-13-1 95356-14-2
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(anteriverto activity of, structure in relation to)

RN 83081-77-0 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



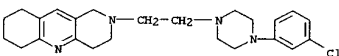
RN 83082-17-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



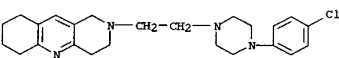
RN 83082-23-9 CAPLUS
CN Benzo[b][1,6]naphthyridine,
1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-

L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

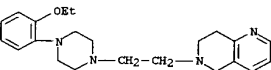
RN 83100-22-5 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



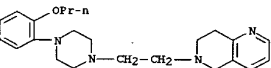
RN 83100-24-7 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-35-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

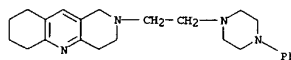


RN 95355-89-8 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-propoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

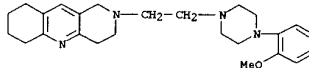


RN 95355-91-2 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-butoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

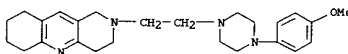
L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl)- (9CI) (CA INDEX NAME)



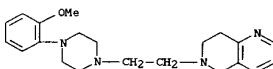
RN 83082-27-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



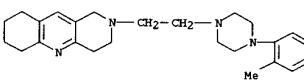
RN 83082-29-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



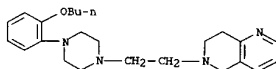
RN 83082-65-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



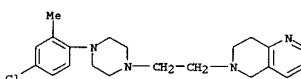
RN 83100-19-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



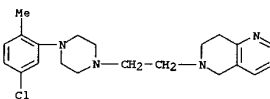
L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



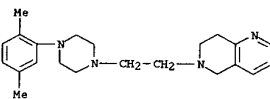
RN 95355-93-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-
5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



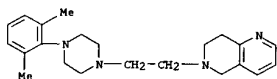
RN 95355-95-6 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(5-chloro-2-methylphenyl)-1-piperazinyl]ethyl]-
5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



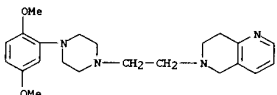
RN 95355-97-8 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



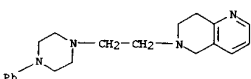
RN 95355-99-0 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



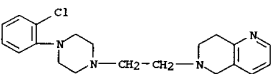
RN 95356-01-7 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2,5-dimethoxyphenyl)-1-piperazinyl]ethyl]-
5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



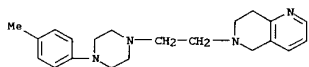
RN 95356-06-2 CAPLUS
CN 1,6-Naphthyridine,
5,6,7,8-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-
(9CI) (CA INDEX NAME)



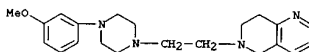
RN 95356-07-3 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)



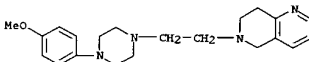
RN 95356-08-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)



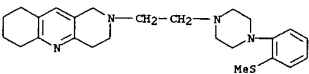
RN 95356-13-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



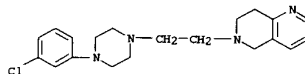
RN 95356-14-2 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



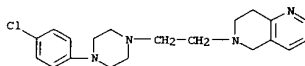
IT 89009-91-6P 101413-03-0P 101413-04-1P
101413-05-2P 101413-06-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antiveritigo activity of, structure in relation to)
RN 89009-91-6 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[2-
(methylthio)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



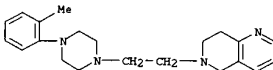
RN 101413-03-0 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-fluorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



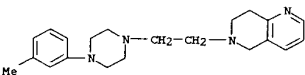
RN 95356-09-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)



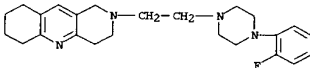
RN 95356-10-8 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



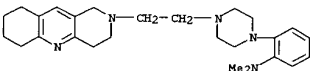
RN 95356-11-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



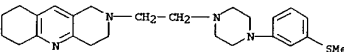
RN 95356-12-0 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



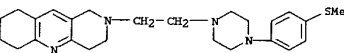
RN 101413-04-1 CAPLUS
CN Benzenamine,
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-
yl)ethyl]-1-piperazinyl]-N,N-dimethyl- (9CI) (CA INDEX NAME)



RN 101413-05-2 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[3-
(methylthio)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

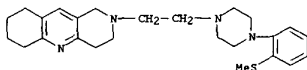


RN 101413-06-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[4-
(methylthio)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



IT 89009-95-0P 101413-07-4P 101413-08-5P
101413-09-6P 101413-10-9P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 89009-95-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[2-
(methylthio)phenyl]-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2)
(9CI) (CA INDEX NAME)

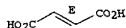
L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CRN 89009-91-6
CMF C25 H34 N4 S



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

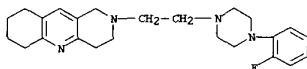
Double bond geometry as shown.



RN 101413-07-4 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-fluorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (ZE)-2-butenedioate (1:2) (9CI) (CA
INDEX NAME)

CM 1

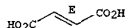
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CM 2

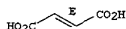
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CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

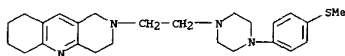


RN 101413-10-9 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(
(methylthio)phenyl)-1-piperazinyl]ethyl]-, (ZE)-2-butenedioate (1:2)
(9CI)

(CA INDEX NAME)

CM 1

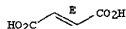
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CMF C25 H34 N4 S



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



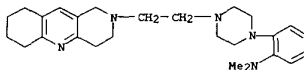
L14 ANSWER 213 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 101413-08-5 CAPLUS
CN Benzenamine,
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-
yl)ethyl]-1-piperazinyl]-N,N-dimethyl-, (ZE)-2-butenedioate (1:2)
(9CI)

(CA INDEX NAME)

CM 1

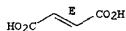
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CMF C26 H37 N5



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

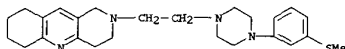


RN 101413-09-6 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-[3-(
(methylthio)phenyl)-1-piperazinyl]ethyl]-, (ZE)-2-butenedioate (1:2)
(9CI)

(CA INDEX NAME)

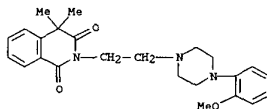
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CMF C25 H34 N4 S



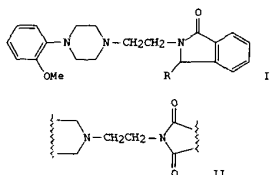
CM 2

L14 ANSWER 214 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:61789 CAPLUS
DOCUMENT NUMBER: 104:61789
TITLE: Further investigations on the
.alpha.1-adrenoceptor
blocking properties of AR-C 239 in rats
AUTHOR(S): Huchet, Anne Marie; Andrejak, Michel; Lucet,
Bernadette; Gautret, Bruno; Doursout, Marie
Francoise;
Ostermann, Gerard; Schmitt, Henri
CORPORATE SOURCE: Dep. Pharmacol., Fac. Med. Broussais, Paris,
75006,
Fr.
SOURCE: Clin. Exp. Pharmacol. Physiol. (1985), 12(5),
505-13
CODEN: CEXPB9; ISSN: 0305-1870
DOCUMENT TYPE: Journal
LANGUAGE: English
AB AR-C 239 (67339-62-2), an .alpha.-adrenoceptor-blocking drug,
appears to act selectively on .alpha.1 sites in rats. At peripheral
sites, this drug did not change the tachycardia induced by spinal
sympathetic outflow stimulation in pithed rats, and did not
antagonize the
inhibitory effects of clonidine on this prep. In addn., AR-C 239
showed
predominant .alpha.1-adrenoceptor-blocking properties in the bisected
rat
vas deferens prep. AR-C 239 did not prevent or reverse the centrally
mediated hypotensive and bradycardic actions induced by clonidine, in
intact animals. Thus, AR-C 239 seems to be a very useful tool for the
characterization of peripheral and central .alpha.1-adrenoceptors, in
this
animal species.
IT 67339-62-2
RL: BIOL (Biological study)
(as .alpha.1-sympatholytic)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



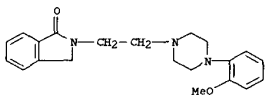
L14 ANSWER 215 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1986:34108 CAPLUS
 DOCUMENT NUMBER: 104:34108
 TITLE: 2-Methoxyphenylpiperazine derivatives.
 INVENTOR(S): Nagano, Hiroyuki; Takagi, Michiro; Kubodera, Noboru;
 Matsunaga, Isao; Nabata, Hiroyuki; Oba, Yasuhiro;
 Sakai, Kazunari; Uchida, Yasuyoshi
 Chugai Pharmaceutical Co., Ltd., Japan
 Jpn. Kokai Tokkyo Koho, 2 pp.
 CODEN: JXXXXF
 LANGUAGE: Patent
 Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:
 PATENT NO. KIND DATE APPLICATION NO. DATE

 JF 60169461 A2 19850902 JF 1984-24074 19840210
 JF 03053301 B4 19910814
 OTHER SOURCE(S): CASREACT 104:34108
 GI

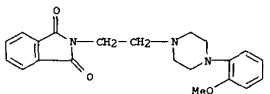


AB Title compds. I (R = H, OH) and their salts, useful as cardiovascular agents (no data), were prepd. Thus, stirring 2.88 g II and 800 mg NaBH₄ in MeOH at room temp. for 5 h gave 2.3 g I (R = OH).
 IT 99718-68-09 99718-69-19 99718-70-49
 99718-71-59
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of, as cardiovascular agent)
 RN 99718-68-0 CAPLUS
 CN 1H-Isocindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

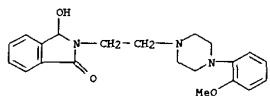
L14 ANSWER 215 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



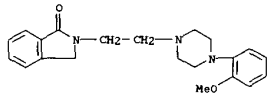
● x HCl
 IT 99718-67-9
 RL: RCI (Reactant)
 (redn. of, with sodium borohydride)
 RN 99718-67-9 CAPLUS
 CN 1H-Isocindole-1,3(2H)-dione,
 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-
 (9CI) (CA INDEX NAME)



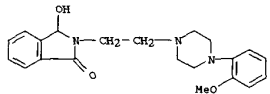
L14 ANSWER 215 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 99718-69-1 CAPLUS
 CN 1H-Isocindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 99718-70-4 CAPLUS
 CN 1H-Isocindol-1-one, 2,3-dihydro-3-hydroxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

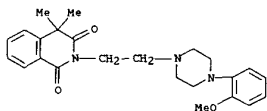


● x HCl

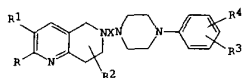
RN 99718-71-5 CAPLUS
 CN 1H-Isocindol-1-one, 2,3-dihydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 216 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1985:49213 CAPLUS
 DOCUMENT NUMBER: 103:9213
 TITLE: [3H]-Rauwolfscine binding to
 .alpha.2-adrenoceptors in
 the mammalian kidney: apparent receptor
 heterogeneity
 between species
 AUTHOR(S): Neylon, C. B.; Summers, R. J.
 CORPORATE SOURCE: Dep. Pharmacol., Univ. Melbourne, Parkville, 3052,
 Australia
 SOURCE: Br. J. Pharmacol. (1985), 85(2), 349-59
 CODEN: BJPCMH; ISSN: 0007-1188
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Binding of the .alpha.2-adrenoceptor antagonist 3H-labeled rauwolfscine
 [131-03-3] was characterized in membrane preps. from the kidneys of
 mouse, rat, rabbit, dog, and man. In all species, binding reached
 equil. within 45 min and dissocd. at a single exponential rate after addn. of
 phentolamine 10 .mu.M. Satn. studies showed that the affinity of
 [3H]rauwolfscine was similar in all species (2.33-3.03 nM) except man
 where it was higher (0.98 nM). Marked differences were seen in the d. of
 binding sites, increasing in the order: man < dog < rabbit < rat <
 mouse.
 In all cases, Hill coeffs. were not different from unity.
 [3H]rauwolfscine binds with low affinity (dissocn. const. KD > 15 nM) to membranes
 prepd. from guinea-pig kidney. The low affinity binding is not due to the
 absence of particular ions in the incubation medium or to receptor
 occupation by endogenous agonist. The binding in all species was
 stereoselective with respect to the isomers of noradrenaline.
 However, differences were seen in the characteristics of agonist interactions
 with the binding site both between isomers and between species. Marked
 differences in affinity of particular .alpha.-adrenoceptor antagonists
 were obsd. for .alpha.2-adrenoceptors labeled by [3H]rauwolfscine.
 These differences were most evident with the .alpha.1-adrenoceptor selective
 antagonist prazosin [19216-56-9] which displayed inhibition constns.
 (Ki values) of 33.2, 39.5, 261, 570, and 595 nM in rat, mouse, dog, man,
 and rabbit, resp. Differences are apparent in the characteristics of
 .alpha.2-adrenoceptors labeled by [3H]rauwolfscine between species and
 the differences obsd. for .alpha.1-selective antagonists such as prazosin
 may be related to binding to addnl. sites in the vicinity of the
 .alpha.2-adrenoceptor.
 IT 67339-62-2
 RL: BIOL (Biological study)
 (.alpha.2-adrenoceptor binding of, in kidney of human and lab.
 animals,

L14 ANSWER 216 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 Species Variations in)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1385:149226 CAPLUS
 DOCUMENT NUMBER: 102:149226
 TITLE: Antivertigo agents. IV. Synthesis and activity of 6-[.omega.-(4-aryl-1-piperazinyl)alkyl]-5,6,7,8-tetrahydro-1,6-naphthyridines
 AUTHOR(S): Shiozawa, Akira; Ichikawa, Yuhichiro; Komuro, Chikara;
 Ishikawa, Michio; Furuta, Yasuhiko; Kurasahige, Shuji;
 Miyazaki, Hiroshi; Yamanaka, Hiroshi; Sakamoto, Takao
 CORPORATE SOURCE: Res. Lab. Pharm. Div., Nippon Kayaku Co., Tokyo, 115,
 SOURCE: Japan Chem. Pharm. Bull. (1984), 32(10), 3981-93
 CODEN: CPBTAL; ISSN: 0009-2363
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



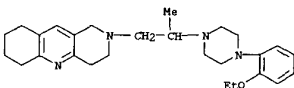
AB 6-[.omega.-(4-Aryl-1-piperazinyl)alkyl]-5,6,7,8-tetrahydro-1,6-naphthyridines I [R, R1 = H, Me; RR1 = (CH2)4; R2 = H, 5-Me 7-Me, 8-Me; R3 = H, F, Cl, Me, alkoxy; R4 = H, Cl, Me, OMe; X = alkylene] (50 compds.) were synthesized and evaluated for antivertigo activity by testing their ability to inhibit spontaneous nystagmus in cats. Structure-activity relationships are discussed. Many I having the 4-(2-alkoxyphenyl)piperazine group showed more potent antivertigo activity than diphenidol. Among them, I [RR1 = (CH2)4, R2 = R4 = H, R3 = 2-Eto, X = CH2CH2] was selected as a promising antivertigo agent. This compd. also exhibited a more potent inhibitory effect on apomorphine-induced vomiting in dogs than diphenidol.
 IT 83081-59-8P 83081-71-4P 83081-72-5P
 83081-73-6P 83081-76-9P 83081-77-0P
 83081-78-1P 83082-17-1P 83082-18-2P
 83082-23-9P 83082-24-0P 83082-27-3P
 83082-28-4P 83082-29-5P 83082-30-8P
 83082-37-5P 83082-38-6P 83082-59-1P
 83082-61-5P 83082-62-6P 83082-65-9P

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

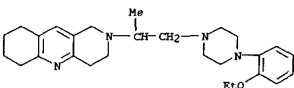
83082-67-1P 83100-13-4P 83100-14-5P
 83100-17-8P 83100-18-9P 83100-19-0P
 83100-20-3P 83100-22-5P 83100-23-6P
 83100-24-7P 83100-25-8P 83100-35-0P
 83100-36-1P 84328-17-6P 95355-89-8P
 95355-90-1P 95355-91-2P 95355-92-3P
 95355-93-4P 95355-94-5P 95355-95-6P
 95355-96-7P 95355-97-8P 95355-98-9P
 95355-99-0P 95356-00-6P 95356-01-7P
 95356-02-8P 95356-03-9P 95356-04-0P
 95356-05-1P 95356-06-2P 95356-07-3P
 95356-08-4P 95356-09-5P 95356-10-6P
 95356-11-9P 95356-12-0P 95356-13-1P
 95356-14-2P 95395-61-2P 95395-62-3P
 95395-63-4P 95395-64-5P 95395-65-6P
 95395-66-7P 95395-67-8P 95395-68-9P
 95410-22-3P

RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and antivertigo activity of)

RN 83081-59-8 CAPLUS
 CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



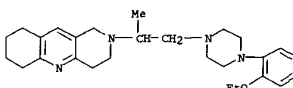
RN 83081-71-4 CAPLUS
 CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83081-72-5 CAPLUS
 CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

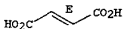
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CH 1
 CRN 83081-71-4
 CMF C27 H38 N4 O

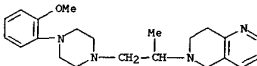


CH 2
 CRN 110-17-8
 CMF C4 H4 O4
 CUES 2:E

Double bond geometry as shown.



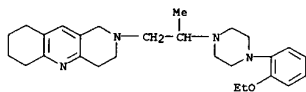
RN 83081-73-6 CAPLUS
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)



RN 83081-76-9 CAPLUS
 CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-1,2,3,4,6,7,8,9-octahydro-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

CH 1
 CRN 83081-59-8
 CMF C27 H38 N4 O

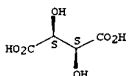
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



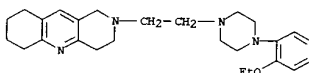
CH 2

CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.



RN 83081-77-0 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83081-78-1 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

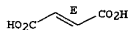
CH 1

CRN 83081-77-0
CMF C26 H36 N4 O

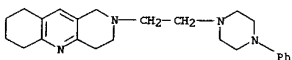
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



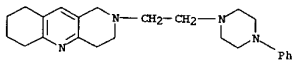
RN 83082-23-9 CAPLUS
CN Benzo[b][1,6]naphthyridine,
1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(phenyl-1-
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83082-24-0 CAPLUS
CN Benzo[b][1,6]naphthyridine,
1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(phenyl-1-
piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

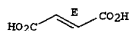
CRN 83082-23-9
CMF C24 H32 N4



CH 2

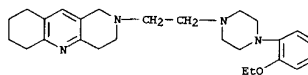
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-27-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

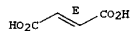
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



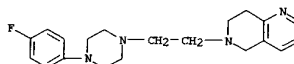
CH 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



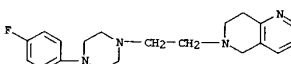
RN 83082-17-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)



RN 83082-18-2 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

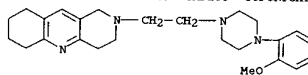
CRN 83082-17-1
CMF C20 H25 F N4



CH 2

CRN 110-17-8

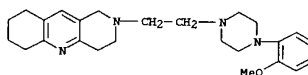
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 83082-28-4 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)
(CA INDEX NAME)

CH 1

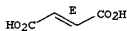
CRN 83082-27-3
CMF C25 H34 N4 O



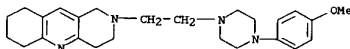
CH 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-29-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

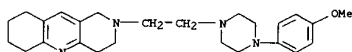


RN 83082-30-8 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)
(CA INDEX NAME)

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CH 1

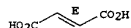
CRN 83082-29-5
CMF C25 H34 N4 O



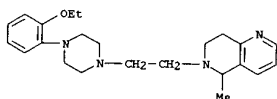
CH 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-37-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-methyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)



RN 83082-38-6 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-methyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI)
(CA INDEX NAME)

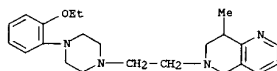
CH 1

CRN 83082-37-5
CMF C23 H32 N4 O

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CH 1

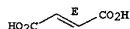
CRN 83082-61-5
CMF C23 H32 N4 O



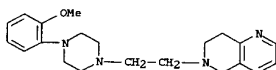
CH 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-65-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83082-67-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

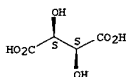
CRN 83082-65-9
CMF C21 H28 N4 O

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

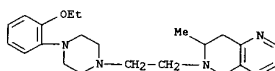
CH 2

CRN 133-37-9
CMF C4 H6 O6

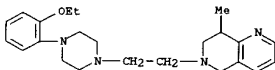
Relative stereochemistry.



RN 83082-59-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-7-methyl-, (9CI) (CA INDEX NAME)

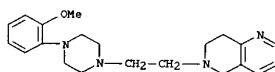


RN 83082-61-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-8-methyl-, (9CI) (CA INDEX NAME)



RN 83082-62-6 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-

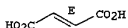
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



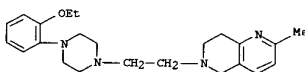
CH 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



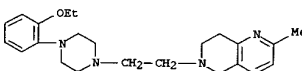
RN 83100-13-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-2-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)



RN 83100-14-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-2-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

CRN 83100-13-4
CMF C23 H32 N4 O

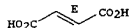


CH 2

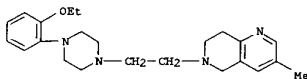
CRN 110-17-8

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.



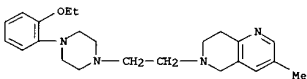
RN 83100-17-8 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-3-methyl- (9CI) (CA INDEX NAME)



RN 83100-18-9 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

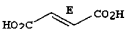
CRN 83100-17-8
 CMF C23 H32 N4 O



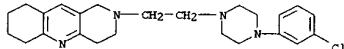
CM 2

CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.



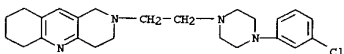
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 83100-23-6 CAPLUS
 CN Benzo[b][1,6]naphthyridine,
 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

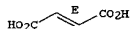
CRN 83100-22-5
 CMF C24 H31 Cl N4



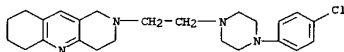
CM 2

CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.

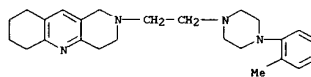


RN 83100-24-7 CAPLUS
 CN Benzo[b][1,6]naphthyridine,
 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
 1,2,3,4,6,7,8,9-octahydro-, (9CI) (CA INDEX NAME)



RN 83100-25-8 CAPLUS
 CN Benzo[b][1,6]naphthyridine,
 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

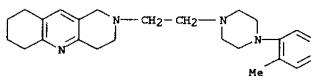
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 83100-19-0 CAPLUS
 CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83100-20-3 CAPLUS
 CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

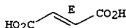
CRN 83100-19-0
 CMF C25 H34 N4



CM 2

CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.

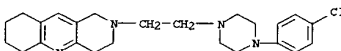


RN 83100-22-5 CAPLUS
 CN Benzo[b][1,6]naphthyridine,
 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
 1,2,3,4,6,7,8,9-octahydro-, (9CI) (CA INDEX NAME)

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CM 1

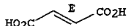
CRN 83100-24-7
 CMF C24 H31 Cl N4



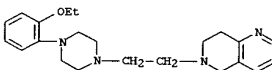
CM 2

CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.



RN 83100-35-0 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-, (9CI) (CA INDEX NAME)

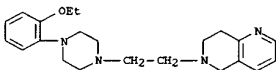


RN 83100-36-1 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83100-35-0
 CMF C22 H30 N4 O

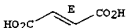
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

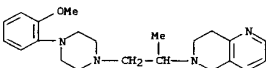
Double bond geometry as shown.



RN 84328-17-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[(4-(2-methoxyphenyl)-1-piperazinyl)-1-methylethyl]-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

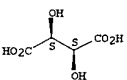
CRN 83081-73-6
CMF C22 H30 N4 O



CM 2

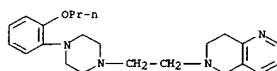
CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.



RN 95355-89-8 CAPLUS

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[(4-(2-propoxyphenyl)-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

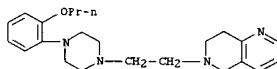


RN 95355-90-1 CAPLUS

CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[(4-(2-propoxyphenyl)-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

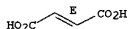
CRN 95355-89-8
CMF C23 H32 N4 O



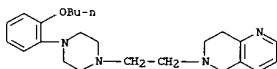
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 95355-91-2 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[(4-(2-butoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



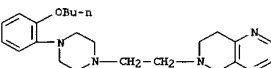
RN 95355-92-3 CAPLUS

CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[(4-(2-butoxyphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

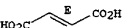
CRN 95355-91-2
CMF C24 H34 N4 O



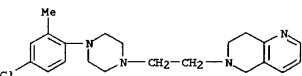
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 95355-93-4 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[(4-(4-chloro-2-methylphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

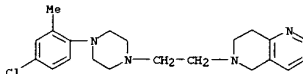


RN 95355-94-5 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[(4-(4-chloro-2-methylphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95355-93-4
CMF C21 H27 Cl N4

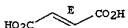
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



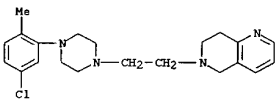
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 95355-95-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[(4-(5-chloro-2-methylphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

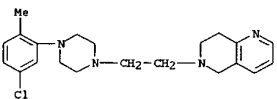


RN 95355-96-7 CAPLUS

CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[(4-(5-chloro-2-methylphenyl)-1-piperazinyl)ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95355-95-6
CMF C21 H27 Cl N4

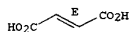


L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

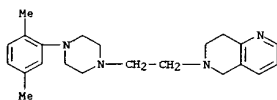
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



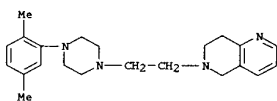
RN 95355-97-8 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



RN 95355-98-9 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95355-97-8
CMF C22 H30 N4

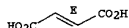


CM 2

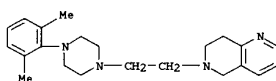
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



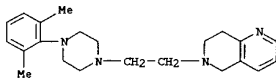
RN 95355-99-0 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)



RN 95356-00-6 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

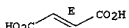
CRN 95355-99-0
CMF C22 H30 N4



CM 2

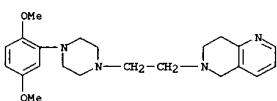
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 95356-01-7 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)

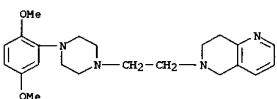
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 95356-02-8 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2,5-dimethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

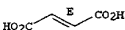
CRN 95356-01-7
CMF C22 H30 N4 O2



CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

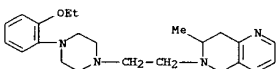


RN 95356-03-9 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-methyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 83082-59-1
CMF C23 H32 N4 O

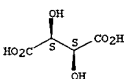
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



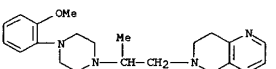
CM 2

CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.



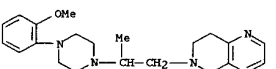
RN 95356-04-0 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]- (9CI) (CA INDEX NAME)



RN 95356-05-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]propyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

CRN 95356-04-0
CMF C22 H30 N4 O

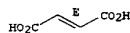


CM 2

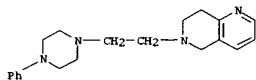
CRN 110-17-8

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CMF C4 H4 O4
 CDES 2:E

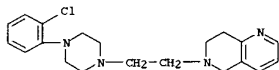
Double bond geometry as shown.



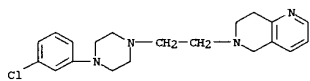
RN 95356-06-2 CAPLUS
 CN 1,6-Naphthyridine,
 5,6,7,8-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-
 (9CI) (CA INDEX NAME)



RN 95356-07-3 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro- (9CI) (CA INDEX NAME)

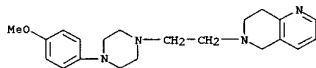


RN 95356-08-4 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro- (9CI) (CA INDEX NAME)



RN 95356-09-5 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro- (9CI) (CA INDEX NAME)

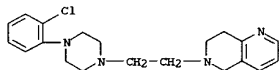
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methoxyphenyl)-1-
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 95395-61-2 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

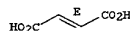
CRN 95356-07-3
 CMF C20 H25 Cl N4



CM 2

CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.

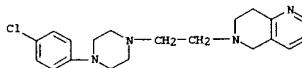


RN 95395-62-3 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

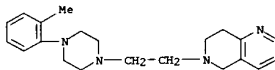
CM 1

CRN 95356-08-4
 CMF C20 H25 Cl N4

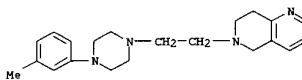
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



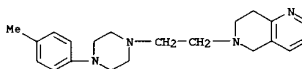
RN 95356-10-8 CAPLUS
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methylphenyl)-1-
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



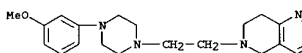
RN 95356-11-9 CAPLUS
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methylphenyl)-1-
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 95356-12-0 CAPLUS
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(4-methylphenyl)-1-
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

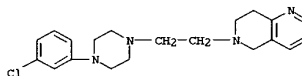


RN 95356-13-1 CAPLUS
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(3-methoxyphenyl)-1-
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 95356-14-2 CAPLUS

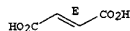
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



CM 2

CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

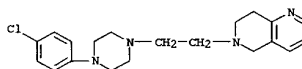
Double bond geometry as shown.



RN 95395-63-4 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

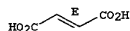
CRN 95356-09-5
 CMF C20 H25 Cl N4



CM 2

CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

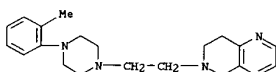
Double bond geometry as shown.



RN 95395-64-5 CAPLUS
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methylphenyl)-1-
 piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

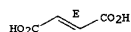
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CH 1
CRN 95356-10-8
CMF C21 H28 N4



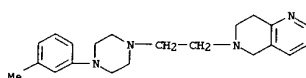
CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 95395-65-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-{4-(3-methylphenyl)-1-piperazinyl}ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1
CRN 95356-11-9
CMF C21 H28 N4

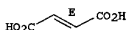


CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

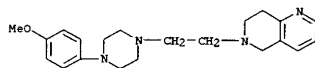
L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CDES 2:E

Double bond geometry as shown.



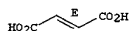
RN 95395-68-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-{4-(4-methoxyphenyl)-1-piperazinyl}ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1
CRN 95356-14-2
CMF C21 H28 N4 O



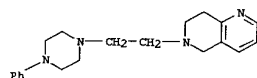
CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

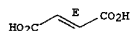


RN 95410-22-3 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1
CRN 95356-06-2
CMF C20 H26 N4

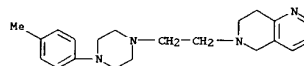


L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



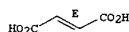
RN 95395-66-7 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-{4-(4-methylphenyl)-1-piperazinyl}ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1
CRN 95356-12-0
CMF C21 H28 N4



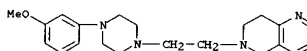
CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 95395-67-8 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-{4-(3-methoxyphenyl)-1-piperazinyl}ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1
CRN 95356-13-1
CMF C21 H28 N4 O



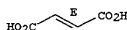
CH 2
CRN 110-17-8
CMF C4 H4 O4

L14 ANSWER 217 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

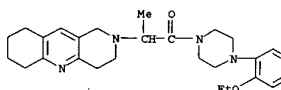
CH 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

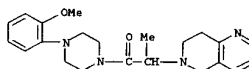
Double bond geometry as shown.



IT 83099-95-0P 95395-47-4P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and redn. of)
RN 83099-95-0 CAPLUS
CN Piperazine, 1-(2-ethoxyphenyl)-4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

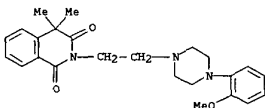


RN 95395-47-4 CAPLUS
CN Piperazine, 1-(2-ethoxyphenyl)-4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)

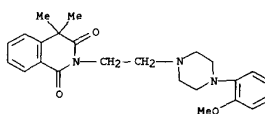


L14 ANSWER 218 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1985:73242 CAPLUS
 DOCUMENT NUMBER: 102:73242
 TITLE: Calcium influx-dependent and -independent .alpha.1-adrenoceptor-mediated processes of vasoconstriction in vivo do not operate via different .alpha.1-adrenoceptor subtypes
 AUTHOR(S): Korstanje, Cornelis; Wilffert, Bob; De Jonge, Adriaan; Thoolen, Martin J. M. C.; Timmermans, Pieter B. M.; Van Zwieten, Pieter A.
 CORPORATE SOURCE: Dep. Pharm., Univ. Amsterdam, Amsterdam, 1018 TV, Neth.
 SOURCE: J. Cardiovasc. Pharmacol. (1984), 6(6), 1102-8
 CODEN: JCPEDT; ISSN: 0160-2446
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In pithed rats, the selective .alpha.1-adrenoceptor agonists St 587 [15327-38-5] and cirazoline [59939-16-1] show preponderant Ca influx-dependent and -independent vasoconstriction, resp. Using these agonists, selective (competitive) antagonists for either process of vasoconstriction were sought. For this purpose, antagonism was analyzed for 8 structurally different antagonists (prazosin [19216-56-9], BE 2254 [40077-13-2], AR-C239 [67339-62-2], R 28935 [55806-43-4], corynanthine [483-10-3], phentolamine [50-60-2], sulpiride [15676-16-1], and chlorpromazine [50-53-3]) opposing the pressor responses evoked by cirazoline and St 587. Where pA2 values (-log dose antagonist evoking a 2-fold shift for the agonist dose-response curve) could be calcd., no significantly different pA2 values against either agonist resulted. However, with respect to the slopes of the Schild plots, deviations from 1 were found for prazosin, R 28935, AR-C239, sulpiride, and chlorpromazine, but not uniformly against both agonists. Following treatment with phenoxybenzamine (PB) (30 .mu.g/kg) and nifedipine (1 mg/kg), which produced Ca influx-sensitive and -insensitive vasoconstriction to cirazoline, resp., Schild plots were constructed for BE 2254, prazosin, and chlorpromazine. Using cirazoline as an agonist, unity slopes were now obtained for prazosin and chlorpromazine. The Schild plots of BE 2254 vs. cirazoline after PB or nifedipine administration, however, exhibited a slope deviating from 1. For prazosin and chlorpromazine, identical pA2 values still resulted against both processes of vasoconstriction to cirazoline. Evidently, .alpha.1-adrenoceptors mediating Ca influx-dependent and -independent vasoconstriction in vivo are not distinctly different entities, but are sep. recognition sites of the same receptor.

L14 ANSWER 219 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1984:604190 CAPLUS
 DOCUMENT NUMBER: 101:204190
 TITLE: Non-specific, time-dependent desensitization of the rat vas deferens and anococcygeus preparations of .alpha.1-adrenoceptor antagonists and atropine
 AUTHOR(S): Onnen, Igor
 CORPORATE SOURCE: Fac. Med., Univ. Paris-Nord, Bobigny, Fr.
 SOURCE: Br. J. Pharmacol. (1984), 93(1), 7-14
 CODEN: BJPCDH; ISSN: 0007-1188
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Rat vas deferens preps. became desensitized to the .alpha.1-adrenoceptor antagonist thymoxamine [54-32-0]: after 6 h in vitro, the 4 value (time to attain half the occupancy of receptors occupied at equil.) of the response to this drug was 1.50 fold greater in control strips (strips exposed to thymoxamine at 6 h) than in test strips (strips exposed to thymoxamine at 1 h). The rate of action of the .alpha.1-adrenoceptor antagonist AR-C239 [67339-62-2] on the rat anococcygeus prep. was correlated with the rate of action of atropine [51-55-8]. There was also a significant correlation between the 4 ratios (1.37 and 1.30 for AR-C239 an atropine resp.) obsd. in the control muscles at 6 h. The in vitro slowing is thus due to some change in the longitudinal muscle and not to a change in the receptors. The in vitro slowing occurred when either phenylephrine or methoxamine was the .alpha.1-adrenoceptor agonist used. The most likely mechanism of desensitization is a non-specific slowing of the access of drugs to receptors.
 IT 67339-62-2
 RL: BIOL (Biological study)
 (vas deferens and anococcygeus muscle desensitization to)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



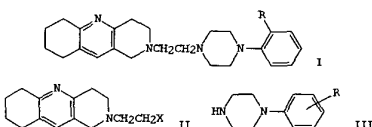
L14 ANSWER 218 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 IT 67339-62-2
 RL: BIOL (Biological study)
 (blood vessel contraction inhibition by, adrenergic receptors and calcium in relation to)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 220 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1984:103395 CAPLUS
 DOCUMENT NUMBER: 100:103395
 TITLE: 1,2,3,4,6,7,8,9-Octahydro-benzo[b],1,6-naphthyridine derivatives
 PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
 CODEN: JXXXXF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

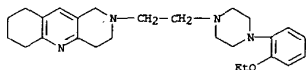
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 58188884 | A2 | 19831104 | JP 1982-70338 | 19820428 |

G1

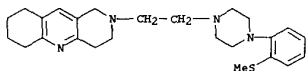


AB Title compds. I (R = MeS, EtO, BzO) were prepd. by reaction of II (X = halo) with III (R = MeS, EtO) optionally followed by hydrolysis and benzoylation. Antivertigo and muscle relaxation activity test data of I were shown in cats and mice, resp. Thus, refluxing a mixt. of II 2HCl (X = Cl) 4.9, III HCl (R = O-MeS) 3.7, and Et3N 7.6 g in EtOH 2 h gave 76% I (R = MeS), which was converted to the fumarate by treating with fumaric acid in Me2CO.
 IT 83081-77-0P 89009-91-6P 89009-92-7P
 89009-94-9P 89009-95-0P 89009-96-1P
 RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. and pharmacol. activities of)
 RN 83081-77-0 CAPLUS
 CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)

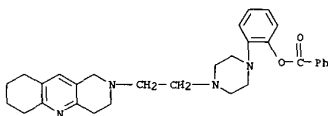
L14 ANSWER 220 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 89009-91-6 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(methylthio)phenyl]-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 89009-92-7 CAPLUS
CN Phenol,
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)ethyl]-1-piperazinyl]-, benzoate (ester) (9CI) (CA INDEX NAME)

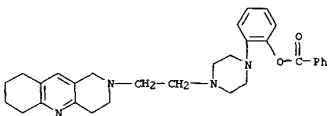


RN 89009-94-9 CAPLUS
CN Phenol,
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)ethyl]-1-piperazinyl]-, benzoate (ester), (2E)-2-butenedioate (1:2) (salt) (9CI) (CA INDEX NAME)

CH 1
CRN 89009-92-7
CMF C31 H36 N4 O2

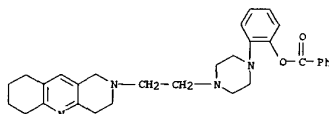
L14 ANSWER 220 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 89009-96-1 CAPLUS
CN Phenol,
2-[4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)ethyl]-1-piperazinyl]-, benzoate (ester), tetrahydrochloride (9CI) (CA INDEX NAME)



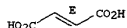
● 4 HCl

L14 ANSWER 220 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



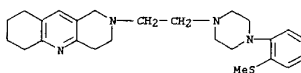
CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



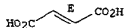
RN 89009-95-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(methylthio)phenyl]-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1
CRN 89009-91-6
CMF C25 H34 N4 S



CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

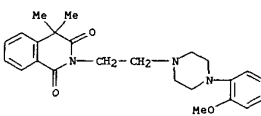
Double bond geometry as shown.



L14 ANSWER 221 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:437179 CAPLUS
DOCUMENT NUMBER: 99:97179
TITLE: Structure of 2-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-1,3(2H,4H)-isoquinolinedione hydrochloride-ethanol (AR-C239), C24H30N3O3+.Cl-.C2H6O
AUTHOR(S): Carpy, Alain; Goursolle, Michel; Leger, Jean
CORPORATE SOURCE: Fac. Pharm., Univ. Bordeaux II, Bordeaux, 33076, Fr.
SOURCE: Acta Crystallogr., Sect. C: Cryst. Struct. Commun. (1983), C39(8), 1087-9
CODEN: ACSCEE
DOCUMENT TYPE: Journal
LANGUAGE: French
AB The title compd. is triclinic, space group P.hivin.1, was a 9.749(2), b 11.287(5), c 13.815(1) .ANG., .alpha. 77.43(2), .beta. 83.99(1), and .gamma. 69.96(3).degree.; 2 = 2 for dc = 1.17. Final R = 0.070 for 2643 reflections. The bridge chain is in the fully extended conformation and is perpendicular to the isoquinoline plane. N-H...Cl H-bonds contribute to the cryst. cohesion. At. coordinates are given.
IT 86891-01-2
RL: PRP (Properties) (structure of)
RN 86891-01-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, monohydrochloride, compd. with ethanol (1:1) (9CI) (CA INDEX NAME)

CH 1
CRN 86891-00-1
CMF C24 H29 N3 O3 . Cl H

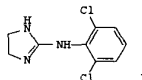


● HCl

L14 ANSWER 221 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CR 2
CRN 64-17-5
CMF C2 H6 O

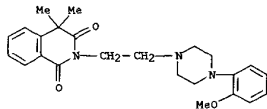
H₃C-CH₂-OH

L14 ANSWER 222 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:432919 CAPLUS
DOCUMENT NUMBER: 99:32919
TITLE: Bronchopulmonary effects of clonidine on the
bronchomotor responses of the guinea pig
AUTHOR(S): Advenier, Charles; Floch, Anne; Mallard, Brigitte
CORPORATE SOURCE: Lab. Pharmacol., Fac. Med. Paris, Paris, F-75270,
Fr.
SOURCE: Eur. J. Pharmacol. (1983), 89(1-2), 85-94
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

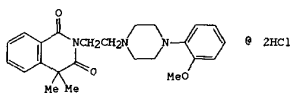


AB In conscious guinea pigs, clonidine (I) [4205-90-7] (10 and 100 .mu.g/kg, i.v.) lowered diastolic (-7.9 and -12.44) and systolic (-8.6 and -11.94) arterial pressure and reduced heart rate (-14.5 and -27.74), but did not significantly modify pulmonary airway resistance. Hypotension was suppressed by yohimbine [146-48-5] and bradycardia was partially suppressed by atropine [51-55-8] and yohimbine, which demonstrates in this animal an .alpha.2-adrenergic effect for hypotension and a mixed cholinergic and .alpha.2-adrenergic effect for bradycardia. Clonidine (10 and 100 .mu.g/kg, i.v.) enhanced the bronchoconstrictor effects of histamine [51-45-6] 20 .mu.g/kg (+80.0 and 89.14), acetylcholine [51-84-3] 25 .mu.g/kg (+66.4 and +95.44) and serotonin creatinine sulfate [971-74-4] 15 .mu.g/kg (+68.5 and +81.44). The duration of this effect was comparable to that of the hypotensive and cardiac effects of clonidine. The effects of clonidines were suppressed after pretreatment with propranolol [525-66-6], reserpine [50-55-5], or pentobarbitone [76-74-4], all drugs which enhance the bronchoconstrictor effect of acetylcholine. Yohimbine (1 mg/kg), piperoxan [59-39-2] (0.3 mg/kg) or prazosin [19216-56-9] in high dosage (0.3 mg/kg) inhibited the potentiation by clonidine of acetylcholine-induced bronchoconstriction, whereas prazosin in lower doses (0.03 mg/kg) or AR-C 239 [67339-62-2] (0.05 mg/kg) had no action. A specific involvement of .alpha.2-adrenoceptors stimulated by clonidine with subsequent redn. of the adrenergic activity assocd. with bronchoespm could therefore be

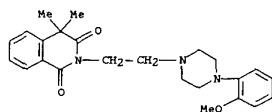
L14 ANSWER 223 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
demonstrated in the conscious guinea-pig during bronchomotor reactions.
IT 67339-62-2
RL: BIOL (Biological study)
(bronchopulmonary effects of clonidine in relation to)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-isquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



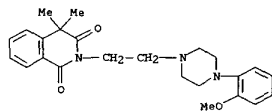
L14 ANSWER 223 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:172852 CAPLUS
DOCUMENT NUMBER: 98:172852
TITLE: AR-C239 a new and potent .alpha.-adrenoceptor
blocker
AUTHOR(S): Mouille, F.; Huchet, A. M.; Chelly, J.; Schmitt, H.
CORPORATE SOURCE: Lab. Pharmacol., Fac. Broussais, Paris, Fr.
SOURCE: Alpha-Bloquants, Symp. Int. (1981), Meeting Date 1979,
14-20. Masson: Paris, Fr.
CODEN: 49LNA7
DOCUMENT TYPE: Conference
LANGUAGE: English
GI



AB The pharmacol. effects of AR-C 239 (I) [67339-62-2] (30-50 mg/kg, i.v.) were investigated in anesthetized dogs. I produced a long-lasting fall in blood pressure and cardiac parameters partly by acting peripherally and partly by central redn. in sympathetic nerve activity. I was specific for .alpha.1-postsynaptic adrenoceptors in dogs. The cardiovascular effects of clonidine and the baroreceptor reflex were unaffected by I, indicating that adrenoceptors implicated in these effects are of the .alpha.2-type. I may be useful in the characterization of .alpha.-adrenoceptors.
IT 67339-62-2
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmacol. of)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-isquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



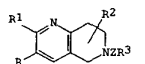
L14 ANSWER 224 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1983:84010 CAPLUS
 DOCUMENT NUMBER: 98:84010
 TITLE: The .alpha.2-adrenergic receptor of human fat cells:
 cells: comparative study of .alpha.2-adrenergic
 radioligand binding and biological response
 AUTHOR(S): Berlan, Michel; Lafontan, Max
 CORPORATE SOURCE: Fac. Med., Univ. Paul Sabatier, Toulouse, F-31400, Fr.
 SOURCE: J. Physiol. (Paris) (1982), 76(3), 279-87
 CODEN: JOPHAN; ISSN: 0021-7948
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The binding of 3H-labeled yohimbine (I) [146-48-5], an .alpha.2-adrenergic antagonist, and clonidine (II) [4205-90-7], an .alpha.2-adrenergic agonist, on the human fat cell membrane .alpha.-adrenoceptor was compared. The relative order of affinity of various agonists and antagonists towards the .alpha.-receptor with their relative biol. potency when estd. by measuring the lipolysis rate of adipocytes in vitro were also compared. The specific binding of these 2 radioactive ligands was a saturable process. The estd. equil. disson. const. (KD) were similar (4 nM for [3H]II, and 4.3 nM for [3H]I). The no. of [3H]I-binding sites per mg protein was .apprx.2-3 times higher than the no. of [3H]II-binding sites (350 fmol/mg protein). The relative order of potency of various .alpha.-agonists and .alpha.-antagonists in competition with the 2 radioligands was similar and was consistent with the delineation of an .alpha.2-adrenoceptor. For integrated anal. at the cellular level, the effect of the various .alpha.-adrenomimetics on theophylline and isoproterenol-induced lipolysis was also studied. Substances which possess .alpha.2-adrenomimetic potency induce an antilipolytic effect whereas .alpha.1-adrenomimetic drugs were without effect. Moreover the order of potency of .alpha.-antagonists in the suppression of the antilipolysis promoted by II is in good agreement with the involvement of an .alpha.2-adrenoceptor stimulation in the genesis of the inhibiting effect on lipolysis. The binding sites of I and II on human fat cell membranes apparently correspond to the physiol. .alpha.2-adrenergic receptors involved in the antilipolytic effect of catecholamines in human adipose tissue.
 IT 67339-62-2
 RL: PROC (Process)
 (adrenergic receptor binding of, in adipocyte of human, lipolysis in relation to)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-



L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1983:72076 CAPLUS
 DOCUMENT NUMBER: 98:72076
 TITLE: 5,6,7,8-Tetrahydro-1,6-naphthyridine derivatives
 INVENTOR(S): Shiozawa, Akira; Ichikawa, Yuhichiro; Ishikawa, Michio; Miyazaki, Hiroshi; Yamanaka, Hiroshi
 PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan
 SOURCE: Fc. Demande, 108 pp.
 CODEN: FRXXBL
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

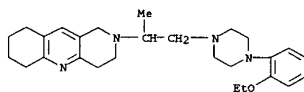
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| FR 2492825 | A1 | 19820430 | FR 1981-20262 | 19811028 |
| JP 57075983 | A2 | 19820512 | JP 1980-150719 | 19801029 |
| ES 507200 | A1 | 19830201 | ES 1981-507200 | 19811029 |

 PRIORITY APPLN. INFO.: JP 1980-150719 19801029
 GI



AB Naphthyridines I (R and R1 are H, alkyl, or RR1 = C2-5 alkylene; R2 = H, alkyl, PhCH2, Ph, halo-, alkyl-, or alkoxyphenyl; Z = C2-4 alkylene;
 R3 = dialkylamine, 1-pyrrolidinyl, 1-piperidinyl, a 4-hydroxy-4-phenyl-1-piperidinyl group, 4-morpholinyl, a 4-substituted 1-piperazinyl group) were prepd., and they showed anti-vertigo and muscle relaxant activity.
 5,6,7,8-Tetrahydro-3-methyl-1,6-naphthyridine was treated with 1-(2-chloroethyl)-4-(2-chlorophenyl)piperazine-ZHCl and Me3N to give I [R = Me, Z = CH2CH2, R3 = 4-(2-chlorophenyl)-1-piperazinyl, R1 = R2 = H].
 IT 83081-72-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and anti-vertigo activity of)
 RN 83081-72-5 CAPLUS
 CN Benzo[h][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (SCI)
 (CA INDEX NAME)

CM 1
 CRN 83081-71-4
 CMF C27 H38 N4 O



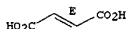
CH 2

CRN 110-17-8

CMF C4 H4 O4

CDES 2:E

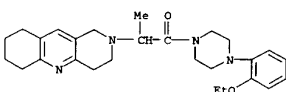
Double bond geometry as shown.



IT 83099-95-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and hydride redn. of)

RN 83099-95-0 CAPLUS

CN Piperazine, 1-(2-ethoxyphenyl)-4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)



IT 83082-18-2P 83082-28-4P 84328-17-6P

RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and muscle relaxant activity of)

RN 83082-18-2 CAPLUS

CN 1,6-Naphthyridine, 6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

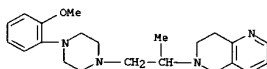
CRN 83082-17-1

CMF C20 H25 F N4

CH 1

CRN 83081-73-6

CMF C22 H30 N4 O

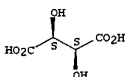


CH 2

CRN 133-37-9

CMF C4 H6 O6

Relative stereochemistry.



IT 83081-75-1P 83082-67-1P 83100-04-3P

83100-14-5P 83100-18-9P 83100-36-1P

83100-40-7P 84345-54-0P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (prepn. and pharmacol. activity of)

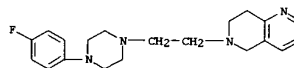
RN 83081-75-1 CAPLUS

CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

CRN 83081-77-0

CMF C26 H36 N4 O



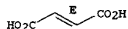
CH 2

CRN 110-17-8

CMF C4 H4 O4

CDES 2:E

Double bond geometry as shown.



RN 83082-28-4 CAPLUS

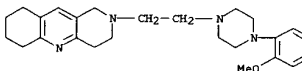
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)

(CA INDEX NAME)

CH 1

CRN 83082-27-3

CMF C25 H34 N4 O



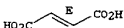
CH 2

CRN 110-17-8

CMF C4 H4 O4

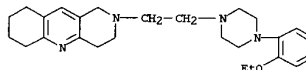
CDES 2:E

Double bond geometry as shown.



RN 84328-17-6 CAPLUS

CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (R*,R*)-2,3-dihydroxybutanedioate (1:2)



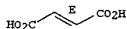
CH 2

CRN 110-17-8

CMF C4 H4 O4

CDES 2:E

Double bond geometry as shown.



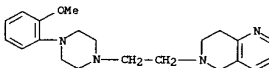
RN 83082-67-1 CAPLUS

CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

CRN 83082-65-9

CMF C21 H29 N4 O



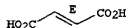
CH 2

CRN 110-17-8

CMF C4 H4 O4

CDES 2:E

Double bond geometry as shown.

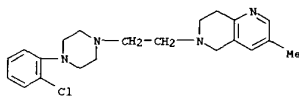


RN 83100-04-3 CAPLUS

CN 1,6-Naphthyridine, 6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

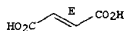
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CH 1
CRN 83100-01-0
CMF C21 H27 Cl N4



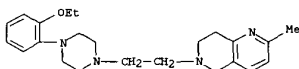
CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83100-14-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-2-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX
NAME)

CH 1
CRN 83100-13-4
CMF C23 H32 N4 O



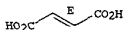
CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

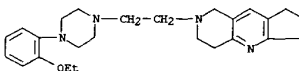
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



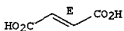
RN 83100-40-7 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-
piperazinyl]ethyl]-2,3,4,6,7,8-hexahydro-, (2E)-2-butenedioate (1:2)
(9CI) (CA INDEX NAME)

CH 1
CRN 83100-39-4
CMF C25 H34 N4 O



CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

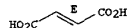
Double bond geometry as shown.



RN 84345-54-0 CAPLUS
CN 1,6-Naphthyridine,
5,6,7,8-tetrahydro-2-methyl-6-[2-[4-(2-methylphenyl)-1-
piperazinyl]ethyl]-, (2E)-2-butenedioate (1:1) (9CI) (CA INDEX NAME)

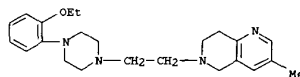
CH 1
CRN 83100-11-2
CMF C22 H30 N4

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



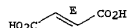
RN 83100-18-9 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1
CRN 83100-17-8
CMF C23 H32 N4 O



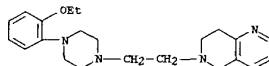
CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



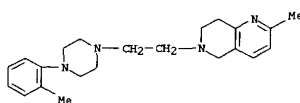
RN 83100-36-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1
CRN 83100-35-0
CMF C22 H30 N4 O



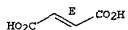
CH 2

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

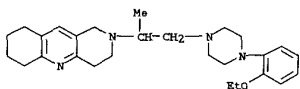


CH 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

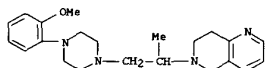
Double bond geometry as shown.



IT 83081-71-4P 83081-73-6P 83081-74-7P
83081-77-0P 83082-17-1P 83082-23-9P
83082-24-0P 83082-27-3P 83082-29-5P
83082-30-8P 83082-31-5P 83082-59-1P
83082-60-4P 83082-61-5P 83082-62-6P
83082-63-7P 83082-64-8P 83082-65-9P
83100-01-0P 83100-11-2P 83100-13-4P
83100-17-8P 83100-19-0P 83100-20-3P
83100-21-4P 83100-22-5P 83100-23-6P
83100-24-7P 83100-25-8P 83100-26-9P
83100-27-0P 83100-35-0P 83100-37-2P
83100-38-3P 83100-39-4P 84414-63-1P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preph. of)
RN 83081-71-4 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-
methylethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



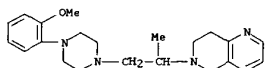
RN 83081-73-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]-1-methylethyl]- (9CI) (CA INDEX NAME)



RN 83081-74-7 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

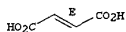
CRN 83081-73-6
CHF C22 H30 N4 O



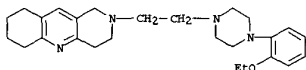
CH 2

CRN 110-17-8
CHF C4 H4 O4
CDES 2:E

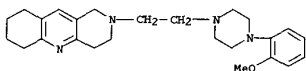
Double bond geometry as shown.



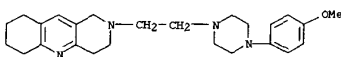
RN 83081-77-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83082-17-1 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)



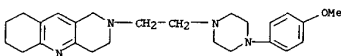
RN 83082-29-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83082-30-8 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

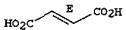
CRN 83082-29-5
CHF C25 H34 N4 O



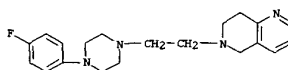
CH 2

CRN 110-17-8
CHF C4 H4 O4
CDES 2:E

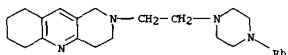
Double bond geometry as shown.



RN 83082-37-5 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-5-methyl-, (9CI) (CA INDEX NAME)



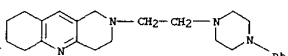
RN 83082-23-9 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-phenyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83082-24-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-phenyl-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CH 1

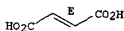
CRN 83082-23-9
CHF C24 H32 N4



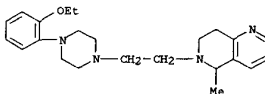
CH 2

CRN 110-17-8
CHF C4 H4 O4
CDES 2:E

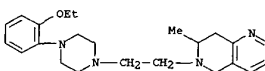
Double bond geometry as shown.



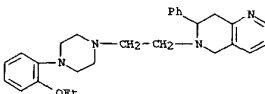
RN 83082-27-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



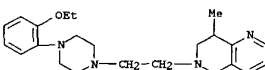
RN 83082-59-1 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-methyl-, (9CI) (CA INDEX NAME)



RN 83082-60-4 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-7-phenyl-, (9CI) (CA INDEX NAME)



RN 83082-61-5 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-methyl-, (9CI) (CA INDEX NAME)

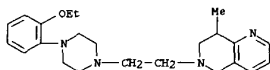


RN 83082-62-6 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-8-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CM 1

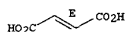
CRN 83082-61-5
CMF C23 H32 N4 O



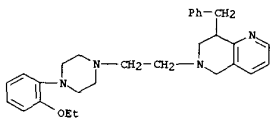
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-63-7 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-8-(phenylmethyl)- (9CI) (CA INDEX NAME)

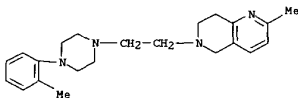


RN 83082-64-8 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-8-(phenylmethyl)-, (2E)-2-butenedioate (1:2) (9CI) (CA
INDEX NAME)

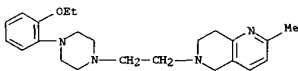
CM 1

CRN 83082-63-7
CMF C29 H36 N4 O

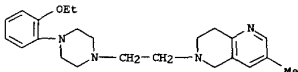
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



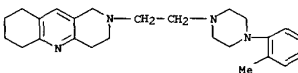
RN 83100-13-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



RN 83100-17-8 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-3-methyl- (9CI) (CA INDEX NAME)

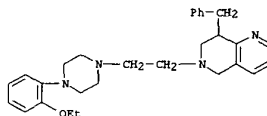


RN 83100-19-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83100-20-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)
(CA

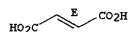
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



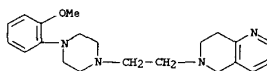
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

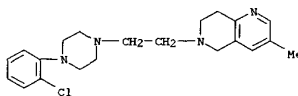
Double bond geometry as shown.



RN 83082-65-9 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 83100-01-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-3-methyl- (9CI) (CA INDEX NAME)

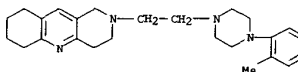


RN 83100-11-2 CAPLUS
CN 1,6-Naphthyridine,
5,6,7,8-tetrahydro-2-methyl-6-[2-[4-(2-methylphenyl)-1-
piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CM 1

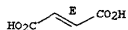
CRN 83100-19-0
CMF C25 H34 N4



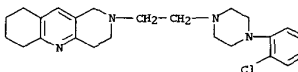
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

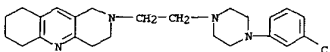
Double bond geometry as shown.



RN 83100-21-4 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



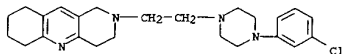
RN 83100-22-5 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-23-6 CAPLUS

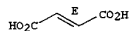
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN Benzo[b][1,6]naphthyridine,
 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA
 INDEX NAME)

CM 1
 CRN 83100-22-5
 CMF C24 H31 Cl N4

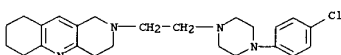


CM 2
 CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.



RN 83100-24-7 CAPLUS
 CN Benzo[b][1,6]naphthyridine,
 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



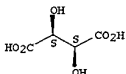
RN 83100-25-8 CAPLUS
 CN Benzo[b][1,6]naphthyridine,
 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA
 INDEX NAME)

CM 1
 CRN 83100-24-7
 CMF C24 H31 Cl N4

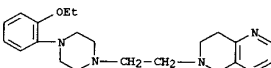
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CM 2
 CRN 133-37-9
 CMF C4 H6 O6

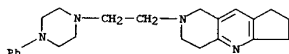
Relative stereochemistry.



RN 83100-35-0 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro- (9CI) (CA INDEX NAME)



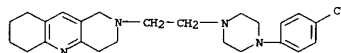
RN 83100-37-2 CAPLUS
 CN 1H-Cyclopenta[b][1,6]naphthyridine,
 2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-
 piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83100-38-3 CAPLUS
 CN 1H-Cyclopenta[b][1,6]naphthyridine,
 2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-
 piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

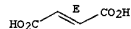
CM 1
 CRN 83100-37-2
 CMF C23 H30 N4

L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

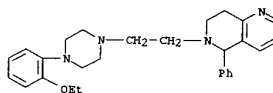


CM 2
 CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.

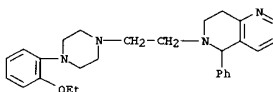


RN 83100-26-9 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-5-phenyl- (9CI) (CA INDEX NAME)

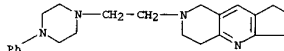


RN 83100-27-0 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-5-phenyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI)
 (CA INDEX NAME)

CM 1
 CRN 83100-26-9
 CMF C28 H34 N4 O

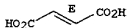


L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

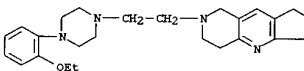


CM 2
 CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.

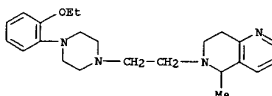


RN 83100-39-4 CAPLUS
 CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-
 piperazinyl]ethyl]-2,3,4,6,7,8-hexahydro- (9CI) (CA INDEX NAME)



RN 84414-63-1 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-5-methyl-, (2R,3R)-2,3-dihydroxybutanedioate (1:2) (9CI)
 (CA INDEX NAME)

CM 1
 CRN 83082-37-5
 CMF C23 H32 N4 O

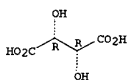


CM 2

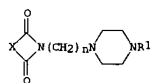
L14 ANSWER 225 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CRN 87-69-4
CMP C4 H6 O6
CDES 1:R2:R*,R*

Absolute stereochemistry.

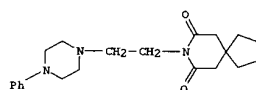


L14 ANSWER 226 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1983:46453 CAPLUS
DOCUMENT NUMBER: 98:46453
TITLE: Buspirone analogs. 1. Structure-activity relationships in a series of N-aryl- and heteroarylpiperazine derivatives
AUTHOR(S): Yevich, J. P.; Temple, D. L., Jr.; New, J. S.; Taylor, Duncan P.; Riblet, L. A.
CORPORATE SOURCE: CNS Res.-Pharm. Res. Dev. Div., Bristol-Myers Co., Evansville, IN, 47721, USA
SOURCE: J. Med. Chem. (1983), 26(2), 194-203
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 98:46453
GI

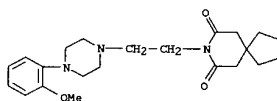


AB The title compds. I (X = substituted cyclic imide; R1 = substituted Ph, substituted pyridyl or substituted pyrimidinyl; n = 2-4) as the HCl salts were prepd. by the reaction of the appropriate piperazinebutanamine with the corresponding cyclic oxy compd. or by the reaction of a substituted piperazine with the corresponding cyclic imide. I and related analogs were tested in vitro for the binding affinities to rat brain membrane sites labeled with either the dopamine antagonist [3H]spiperone or the .alpha.1-adrenergic antagonist [3H]WB-4101 and in vivo for tranquilizing properties and induction of catalepsy. The azaspirodecanedione moiety affords the strongest affinity for dopaminergic binding sites and the most selectivity relative to .alpha.1-adrenergic blocking potential. Structure-activity relations are discussed.
IT 21090-07-3 21102-94-3 21103-20-8
25024-93-5 25024-94-6 83928-69-2
83928-77-2 83928-78-3
RL: BIOL (Biological study)
(anxiolytic and receptor binding activities of)
RN 21090-07-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

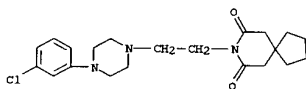
L14 ANSWER 226 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 21102-94-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

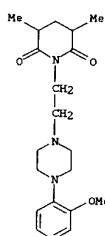


RN 21103-20-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(3-chlorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

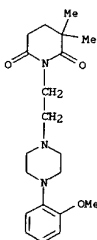


RN 25024-93-5 CAPLUS
CN 2,6-Piperidinedione, 1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-3,5-dimethyl- (9CI) (CA INDEX NAME)

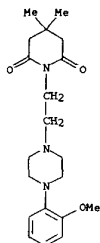
L14 ANSWER 226 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



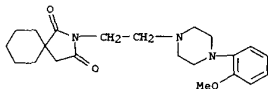
RN 25024-94-6 CAPLUS
CN 2,6-Piperidinedione, 1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-3,3-dimethyl- (9CI) (CA INDEX NAME)



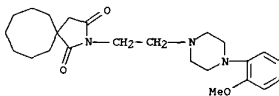
RN 83928-69-2 CAPLUS
CN 2,6-Piperidinedione, 1-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



RN 83928-77-2 CAPLUS
CN 2-Azaspiro[4.5]decane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

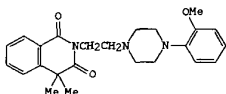


RN 83928-78-3 CAPLUS
CN 2-Azaspiro[4.7]dodecane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

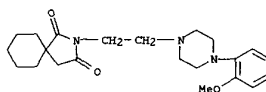


IT 83928-67-0 83928-68-1
RL: BIOL (Biological study)
(pren. and anxiolytic and receptor binding activities of)
RN 83928-67-0 CAPLUS
CN 2-Azaspiro[4.5]decane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

ACCESSION NUMBER: 1983:27864 CAPLUS
DOCUMENT NUMBER: 98:27864
TITLE: Possible role of central .alpha.1-adrenoceptors
in the control of the autonomic nervous system in normotensive and spontaneously hypertensive rats
Ruchet, Anne Marie; Doursout, Marie Françoise;
AUTHOR(S): Chelly, Jacques; Schmitt, Henri
CORPORATE SOURCE: Dep. Pharmacol., Fac. Med. Broussais-Hotel Dieu, Paris, 75006, Fr.
SOURCE: Eur. J. Pharmacol. (1982), 85(2), 239-42
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
GI

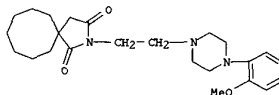


AB The cardiovascular effects of AR-C 239 (I) [67339-62-2], a new and selective .alpha.1-adrenoceptor blocking drug, were studied in normotensive and spontaneously hypertensive rats (SHR). AR-C 239 (300 .mu.g/kg, i.v.) did not change the heart rate in control (without pretreatment) and bilaterally vagotomized normotensive rats, but induced significant bradycardia in rats pretreated with a .beta.1-adrenoceptor blocking drug. The bradycardic effect was inhibited by atropine or bilateral vagotomy. In SHR, the administration of AR-C 239 reduced heart rate in the control, bilaterally vagotomized and .beta.1-blocked rats. Blood pressure was decreased in the same way in the 2 rat strains. Apparently, central .alpha.1-adrenoceptors could participate in the control of vagal tone in normotensive and SH rats, and of sympathetic activity in the SHR only.
IT 67339-62-2
RL: BIOL (Biological study)
(nervous system response to, in hypertension, adrenoceptors in relation to)
RN 67339-62-2 CAPLUS
CN 1,3-bis(2-methoxyphenyl)-2-methyl-2-oxo-1,3-dihydroisquinolin-4-one, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

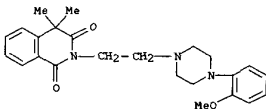


● 2 HCl

RN 83928-68-1 CAPLUS
CN 2-Azaspiro[4.7]dodecane-1,3-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

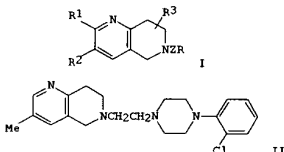


L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1982:544876 CAPLUS
DOCUMENT NUMBER: 97:144876
TITLE: 5,6,7,8-Tetrahydro-1,6-naphthyridine derivatives
INVENTOR(S): Shiozawa, Akira; Ichikawa, Yuhichiro; Ishihawa, Michior Miyazaki, Hiroshi
PATENT ASSIGNEE(S): Nippon Kayaku Co., Ltd., Japan
SOURCE: Ger. Offen., 109 pp.
CODEN: GWXXEX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| DE 3143016 | A1 | 19820527 | DE 1981-3143016 | 19811029 |
| JP 57075983 | A2 | 19820512 | JP 1980-150719 | 19801029 |
| JP 58057379 | A2 | 19830405 | JP 1981-154863 | 19811001 |
| SE 8106359 | A | 19820430 | SE 1981-6359 | 19811028 |
| GB 2087390 | A | 19820526 | GB 1981-32554 | 19811029 |
| GB 2087390 | B2 | 19840613 | | |
| ES 516935 | A1 | 19840216 | ES 1982-516935 | 19821015 |

PRIORITY APPLN. INFO.: JP 1980-150719 19801029
JP 1981-154863 19811001

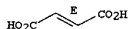
GI



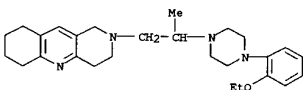
AB The title naphthyridines I [R = dialkylamino, pyrrolidinyl, hydroxyphenylpiperidinyl, 1-morpholinyl, 4-alkyl-, 4-benzyl-, 4-pyridyl-, or 4-(un)substituted-phenylpiperazinyl; R1, R2 = alkyl, R1R2 = C2-5 alkylene; R3 = H, alkyl, Et, R4C6H4 (R4 = H, halo, alkyl, alkoxy); Z = C2-4 alkylene], useful in treatment of vertigo and as muscle relaxants (data tabulated), were prepd. Alkylating 5,6,7,8-tetrahydro-3-methyl-1,6-naphthyridine with 1-(2-chloroethyl)-4-(2-chlorophenyl)piperazine-2HCl in EtOH-NEt3 gave 41% naphthyridine II, which was converted to its difumarate.

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

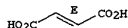


IT 83081-60-1
RL: RCT (Reactant)
(nystagmus inhibitory activity of)
RN 83081-60-1 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA
INDEX NAME)
CM 1
CRN 83081-59-8
CMF C27 H38 N4 O



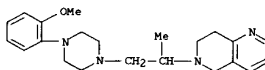
CM 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



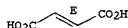
IT 83082-28-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and muscle relaxant activity of)
RN 83082-28-4 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
IT 83081-74-7 83082-18-2
RL: RCT (Reactant)
(muscle relaxant activity of)
RN 83081-74-7 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
CM 1
CRN 83081-73-6
CMF C22 H30 N4 O

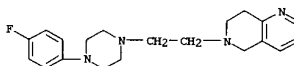


CM 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

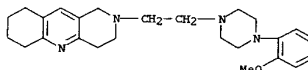


RN 83082-18-2 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
CM 1
CRN 83082-17-1
CMF C20 H25 F N4



CM 2

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CM 1
CRN 83082-27-3
CMF C25 H34 N4 O

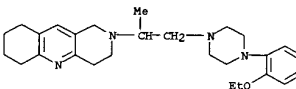


CM 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



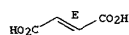
IT 83081-72-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and nystagmus inhibitory activity of)
RN 83081-72-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
CM 1
CRN 83081-71-4
CMF C27 H38 N4 O



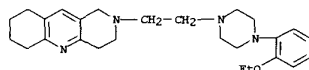
CM 2
CRN 110-17-8
CMF C4 H4 O4

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CDES 2:E

Double bond geometry as shown.

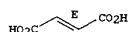


IT 83081-78-1P 83082-67-1P 83100-04-3P
83100-12-3P 83100-14-3P 83100-18-9P
83100-36-1P 83100-40-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and nystagmus inhibitory and muscle relaxant activity of)
RN 83081-78-1 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA
INDEX NAME)
CM 1
CRN 83081-77-0
CMF C26 H36 N4 O



CM 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

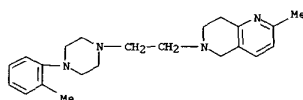
Double bond geometry as shown.



RN 83082-67-1 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
CM 1
CRN 83082-65-9
CMF C21 H28 N4 O

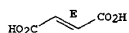
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1
CRN 83100-11-2
CMF C22 H30 N4

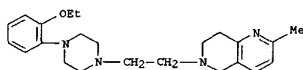


CM 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

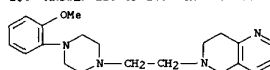


RN 83100-14-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-2-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
CM 1
CRN 83100-13-4
CMF C23 H32 N4 O



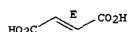
CM 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

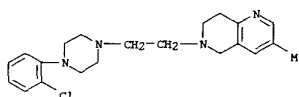


CM 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

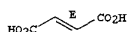


RN 83100-04-3 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
CM 1
CRN 83100-01-0
CMF C21 H27 Cl N4



CM 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

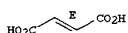
Double bond geometry as shown.



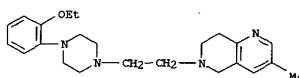
RN 83100-12-3 CAPLUS
CN 1,6-Naphthyridine,
5,6,7,8-tetrahydro-2-methyl-6-[2-[4-(2-methylphenyl)-1-

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

Double bond geometry as shown.

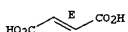


RN 83100-18-9 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-3-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
CM 1
CRN 83100-17-8
CMF C23 H32 N4 O

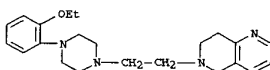


CM 2
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



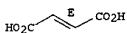
RN 83100-36-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
CM 1
CRN 83100-35-0
CMF C22 H30 N4 O



CM 2

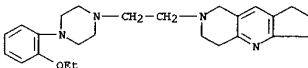
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

RN 83100-40-7 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-2,3,4,6,7,8-hexahydro-, (2E)-2-butenedioate (1:2) (9CI)

(CA INDEX NAME)

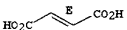
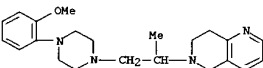
CM 1

CRN 83100-39-4
CMF C25 H34 N4 O

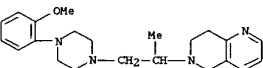
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

IT 83099-95-0P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and redn. of)
RN 83099-95-0 CAPLUS
CN Piperazine, 1-(2-ethoxyphenyl)-4-[2-(3,4,6,7,8,9-hexahydrobenzo[b][1,6]naphthyridin-2(1H)-yl)-1-oxopropyl]- (9CI) (CA INDEX NAME)RN 83081-74-7 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-piperazinyl]-1-methylethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

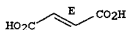
CM 1

CRN 83081-73-6
CMF C22 H30 N4 O

CM 2

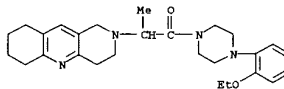
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.

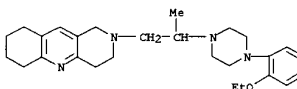
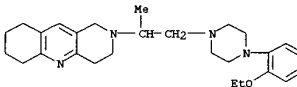
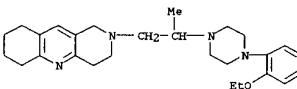
RN 83081-76-9 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-1,2,3,4,6,7,8,9-octahydro-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI)

(CA INDEX NAME)

CM 1

CRN 83081-59-8
CMF C27 H38 N4 OIT 83081-59-8P 83081-71-4P 83081-73-6P
83081-74-7P 83081-76-9P 83081-77-0P
83082-17-1P 83082-23-9P 83082-24-0P
83082-27-3P 83082-29-5P 83082-30-8P
83082-37-5P 83082-38-0P 83082-59-1P
83082-60-4P 83082-61-5P 83082-62-6P
83082-63-7P 83082-64-8P 83082-65-9P
83100-01-0P 83100-11-2P 83100-13-4P
83100-17-8P 83100-19-0P 83100-20-3P
83100-21-4P 83100-22-5P 83100-23-6P
83100-24-7P 83100-25-8P 83100-26-9P
83100-27-0P 83100-35-0P 83100-37-2P
83100-38-3P 83100-39-4P

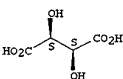
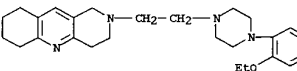
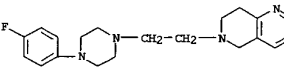
RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

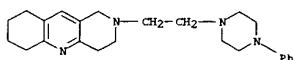
RN 83081-59-8 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]propyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)RN 83081-71-4 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]-1-methylethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)RN 83081-73-6 CAPLUS
CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-

CM 2

CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.

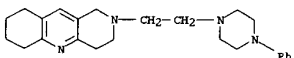
RN 83081-77-0 CAPLUS
CN Benzo[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)RN 83082-17-1 CAPLUS
CN 1,6-Naphthyridine, 6-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-tetrahydro- (9CI) (CA INDEX NAME)RN 83082-23-9 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83082-24-0 CAPLUS
CN Benzo[b][1,6]naphthyridine,
1,2,3,4,6,7,8,9-octahydro-2-[2-(4-phenyl-1-
piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

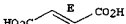
CRN 83082-23-9
CMF C24 H32 N4



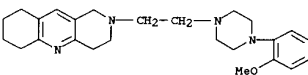
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83082-27-3 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

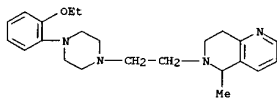


RN 83082-29-5 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-
methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
tetrahydro-5-methyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI)
(CA INDEX NAME)

CM 1

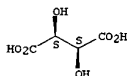
CRN 83082-37-5
CMF C23 H32 N4 O



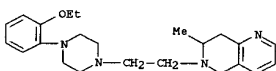
CM 2

CRN 133-37-9
CMF C4 H6 O6

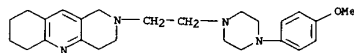
Relative stereochemistry.



RN 83082-59-1 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-7-methyl- (9CI) (CA INDEX NAME)



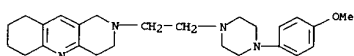
RN 83082-60-4 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-7-phenyl- (9CI) (CA INDEX NAME)



RN 83082-30-8 CAPLUS
CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(4-
methoxyphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)
(CA INDEX NAME)

CM 1

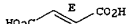
CRN 83082-29-5
CMF C25 H34 N4 O



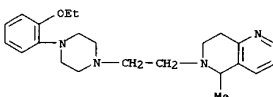
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

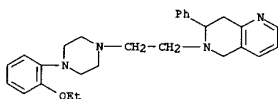
Double bond geometry as shown.



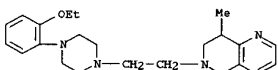
RN 83082-37-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-methyl- (9CI) (CA INDEX NAME)



RN 83082-38-6 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-



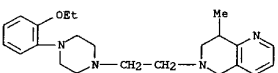
RN 83082-61-5 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-8-methyl- (9CI) (CA INDEX NAME)



RN 83082-62-6 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-8-methyl-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

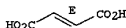
CRN 83082-61-5
CMF C23 H32 N4 O



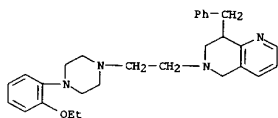
CM 2

CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

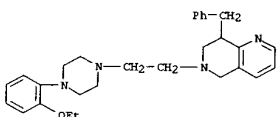
Double bond geometry as shown.



L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 83082-63-7 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-8-(phenylmethyl)- (9CI) (CA INDEX NAME)

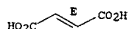


RN 83082-64-8 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-8-(phenylmethyl)-, (2E)-2-butenedioate (1:2) (9CI) (CA
 INDEX
 NAME)
 CH 1
 CRN 83082-63-7
 CMF C29 H36 N4 O



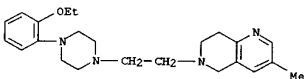
CH 2
 CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.

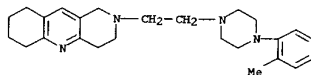


RN 83082-65-9 CAPLUS
 CN 1,6-Naphthyridine, 5,6,7,8-tetrahydro-6-[2-[4-(2-methoxyphenyl)-1-

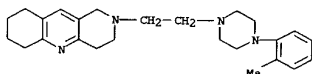
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 tetrahydro-3-methyl- (9CI) (CA INDEX NAME)



RN 83100-19-0 CAPLUS
 CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
 methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

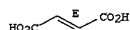


RN 83100-20-3 CAPLUS
 CN Benzo[b][1,6]naphthyridine, 1,2,3,4,6,7,8,9-octahydro-2-[2-[4-(2-
 methylphenyl)-1-piperazinyl]ethyl]-, (2E)-2-butenedioate (1:2) (9CI)
 (CA
 INDEX NAME)
 CH 1
 CRN 83100-19-0
 CMF C25 H34 N4

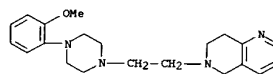


CH 2
 CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

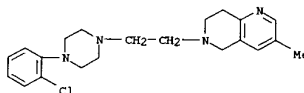
Double bond geometry as shown.



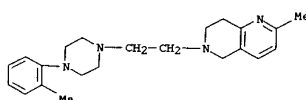
L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



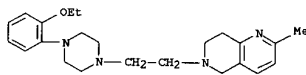
RN 83100-01-0 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-3-methyl- (9CI) (CA INDEX NAME)



RN 83100-11-2 CAPLUS
 CN 1,6-Naphthyridine,
 5,6,7,8-tetrahydro-2-methyl-6-[2-[4-(2-methylphenyl)-1-
 piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



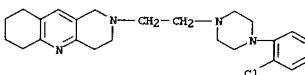
RN 83100-13-4 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
 tetrahydro-2-methyl- (9CI) (CA INDEX NAME)



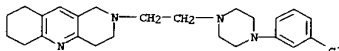
RN 83100-17-8 CAPLUS
 CN 1,6-Naphthyridine,
 6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 83100-21-4 CAPLUS
 CN Benzo[b][1,6]naphthyridine,
 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)

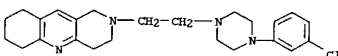


RN 83100-22-5 CAPLUS
 CN Benzo[b][1,6]naphthyridine,
 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
 1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-23-6 CAPLUS
 CN Benzo[b][1,6]naphthyridine,
 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
 1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX
 NAME)

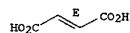
CH 1
 CRN 83100-22-5
 CMF C24 H31 Cl N4



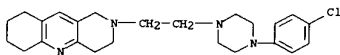
CH 2
 CRN 110-17-8
 CMF C4 H4 O4
 CDES 2:E

Double bond geometry as shown.

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



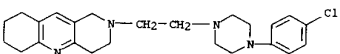
RN 83100-24-7 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro- (9CI) (CA INDEX NAME)



RN 83100-25-8 CAPLUS
CN Benzo[b][1,6]naphthyridine,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
1,2,3,4,6,7,8,9-octahydro-, (2E)-2-butenedioate (1:2) (9CI) (CA
INDEX NAME)

CM 1

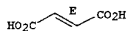
CRN 83100-24-7
CMF C24 H31 Cl N4



CM 2

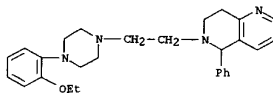
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



RN 83100-26-9 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-phenyl- (9CI) (CA INDEX NAME)

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

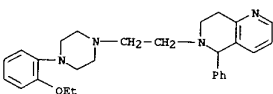


RN 83100-27-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro-5-phenyl-, (R*,R*)-2,3-dihydroxybutanedioate (1:2) (9CI)

(CA INDEX NAME)

CM 1

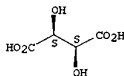
CRN 83100-26-9
CMF C28 H34 N4 O



CM 2

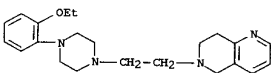
CRN 133-37-9
CMF C4 H6 O6

Relative stereochemistry.

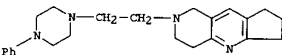


RN 83100-35-0 CAPLUS
CN 1,6-Naphthyridine,
6-[2-[4-(2-ethoxyphenyl)-1-piperazinyl]ethyl]-5,6,7,8-
tetrahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



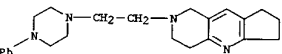
RN 83100-37-2 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine,
2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 83100-38-3 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine,
2,3,4,6,7,8-hexahydro-2-[2-(4-phenyl-1-
piperazinyl)ethyl]-, (2E)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)

CM 1

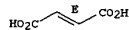
CRN 83100-37-2
CMF C23 H30 N4



CM 2

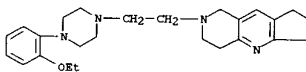
CRN 110-17-8
CMF C4 H4 O4
CDES 2:E

Double bond geometry as shown.



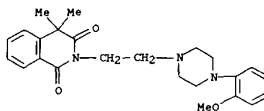
RN 83100-39-4 CAPLUS
CN 1H-Cyclopenta[b][1,6]naphthyridine, 2-[2-[4-(2-ethoxyphenyl)-1-
piperazinyl]ethyl]-2,3,4,6,7,8-hexahydro- (9CI) (CA INDEX NAME)

L14 ANSWER 228 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



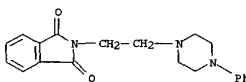
L14 ANSWER 229 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1982:538576 CAPLUS
 DOCUMENT NUMBER: 97:138576
 TITLE: GTP regulates binding of agonists to .alpha.2-adrenergic receptors in human platelets
 AUTHOR(S): Brodde, O. E.; Harding, A.; Ebel, H.; Bock, K. D.
 CORPORATE SOURCE: Med. Klin. Poliklin., Univ. Essen, Essen, D-4300, Fed.
 SOURCE: Rep. Ger. Arch. Int. Pharmacodyn. Ther. (1982), 258(2), 193-207
 DOCUMENT TYPE: CODEN: ALPTAK; ISSN: 0003-9780
 LANGUAGE: English
 AB The potent .alpha.2-adrenergic receptor antagonist 3H-labeled yohimbine [146-48-5] was used to characterize .alpha.-adrenergic receptors in human platelet membranes. Binding of [3H]yohimbine at 25 .degree. was rapid (t1/2 = 3 min), readily reversible (t1/2 = 5.5 min), saturable with 221 fmoles bound/mg protein, and of high affinity (KD = 1.97 nM). Inhibition of binding by .alpha.-adrenergic antagonists showed monophasic displacement curves with Hill-coeffs. of approx. 1.0. The rank order of potency was: rauwolscine [131-03-3] .gtoreq. yohimbine > phenolamine [50-60-2] > phenoxybenzamine [59-96-1] > AR-C 239 [67339-62-2] .gtoreq. corynanthine [483-10-3] > prazosin [19216-56-9], indicating that the .alpha.-adrenergic receptor in human platelets is of the .alpha.2-subtype. On the contrary, agonist clonidine [4205-90-7], guanfacine [29110-47-2], (-)-.alpha.-methylnoradrenaline [829-74-3], (-)-noradrenaline [51-41-2] and (-)-adrenaline [51-43-4]) displacement curves were shallow with Hill-coeffs. of approx. 0.7. Non-linear regression anal. showed that agonists bind to 2 affinity states of the .alpha.2-adrenergic receptor, a high and a low affinity state. In the presence of GTP [86-01-1] (10-14 M) agonist concn.-inhibition curves were shifted to the right to lower affinities and Hill-coeffs. increased up to 1.0. KI values for inhibition of binding in the presence of GTP were in the same range as those for low affinity state in the absence of GTP. Apparently, GTP regulates binding of .alpha.2-adrenergic agonists at the human .alpha.2-adrenergic receptor.
 IT 67339-62-2
 RL: PROC (Process)
 (binding of, to .alpha.-adrenergic receptors of blood platelets of humans)

L14 ANSWER 229 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

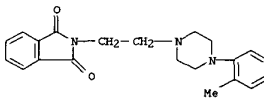


L14 ANSWER 230 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1981:550591 CAPLUS
 DOCUMENT NUMBER: 95:150591
 TITLE: Synthesis and pharmacology of 1-(4-aryl-1-piperazinylalkyl)-4-(4-methoxyphenyl)piperidine-2,6-diones: tranquilizers
 AUTHOR(S): Samant, S. D.; Rulkarni, R. A.
 CORPORATE SOURCE: Dep. Chem., Ramnarain Ruia Coll., Bombay, 400 019, India
 SOURCE: J. Indian Chem. Soc. (1981), 58(7), 692-4
 DOCUMENT TYPE: CODEN: JICSAH; ISSN: 0019-4522
 LANGUAGE: English
 GI

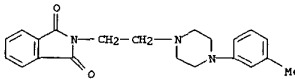
L14 ANSWER 230 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



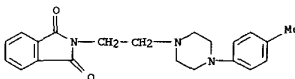
RN 75000-25-8 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



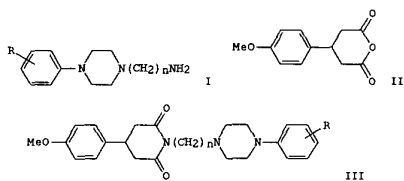
RN 75000-26-9 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-[4-(3-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



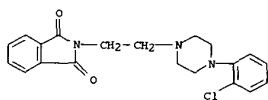
RN 75000-27-0 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



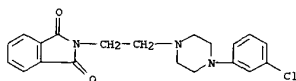
RN 75000-28-1 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



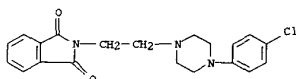
AB Condensation of piperazines I (R = H, 2-, 3-, 4-Me, 2-, 3-, 4-Cl; n = 2, 3) with II gave 24-63% the title compds. (III). III (R = H, n = 2) has an amphetamine antagonist ED50 of 38 mg/kg s.c. in mice.
 IT 75000-24-7 75000-25-8 75000-26-9
 75000-27-0 75000-28-1 75000-29-2
 75000-30-5
 RL: RCT (Reactant)
 (hydrolysis of)
 RN 75000-24-7 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-[4-phenyl-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



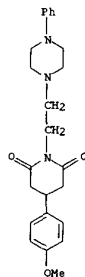
RN 75000-29-2 CAPLUS
CN 1H-Indole-1,3(2H)-dione,
2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)



RN 75000-30-5 CAPLUS
CN 1H-Indole-1,3(2H)-dione,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)

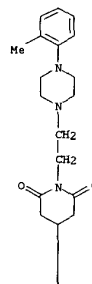


IT 79322-94-4P 79322-95-5P 79322-96-6P
79322-97-7P 79322-98-8P 79322-99-9P
79323-00-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and central nervous system depressant activity of)
RN 79322-94-4 CAPLUS
CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-(4-phenyl-1-
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



RN 79322-95-5 CAPLUS
CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-(4-(2-methylphenyl)-1-
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

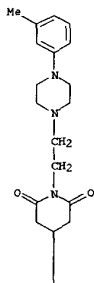
PAGE 1-A



PAGE 2-A

RN 79322-96-6 CAPLUS
CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-(4-(3-methylphenyl)-1-
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

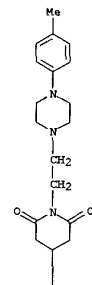


PAGE 2-A



RN 79322-97-7 CAPLUS
CN 2,6-Piperidinedione, 4-(4-methoxyphenyl)-1-[2-(4-(4-methylphenyl)-1-
piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

PAGE 1-A

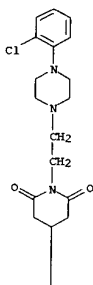


PAGE 2-A



RN 79322-98-8 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4-(4-
methoxyphenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

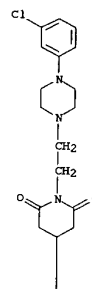


PAGE 2-A



RN 79322-99-9 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-4-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

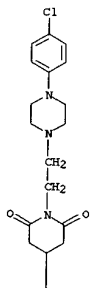


PAGE 2-A



RN 79323-00-5 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-4-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

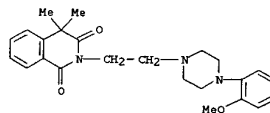
PAGE 1-A



PAGE 2-A



L14 ANSWER 231 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:490956 CAPLUS
DOCUMENT NUMBER: 95:90956
TITLE: Role of .alpha.1- and .alpha.2-adrenoceptors in the modulation of the baroreflex vagal bradycardia
AUTHOR(S): Huchet, Anne Marie; Chelly, Jacques; Schmitt, Henri
CORPORATE SOURCE: Dep. Pharmacol., Fac. Med., Paris, 75270/06, Fr.
SOURCE: Eur. J. Pharmacol. (1981), 71(4), 455-61
CODEN: EJPHAZ; ISSN: 0014-2999
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Yohimbine-HCl [65-19-0] (100 .mu.g/kg), an .alpha.2-adrenoceptor blocking agent when injected into the vertebral artery of anesthetized dogs decreased the vagally mediated bradycardia induced by carotid sinus nerve stimulation. Intracisternal administration of phenylephrine-HCl [61-76-7] (30 .mu.g/kg) an .alpha.1-adrenoceptor agonist decreased, whereas AR-C 239-HCl [78448-19-8] (5 .mu.g/kg) and prazosin-HCl [19237-84-4] (5 .mu.g/kg) 2 potent .alpha.1-adrenoceptor antagonists injected into the vertebral artery, potentiated the bradycardic response. These results suggest, the presence of 2 types of .alpha.-adrenoceptors to modulate the baroreceptor pathway: .alpha.1-adrenoceptors inhibit and .alpha.2-adrenoceptors facilitates the transmission of baroreceptor impulses.
IT 78448-19-8
RL: BIOL (Biological study)
(bradycardia response to, baroreflex in relation to)
RN 78448-19-8 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

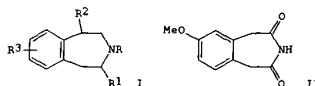


●x HCl

L14 ANSWER 232 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1981:47157 CAPLUS
 DOCUMENT NUMBER: 94:47157
 TITLE: Substituted 1,2,4,5-tetrahydro-3H,3 benzazepines
 INVENTOR(S): Shetty, Bola V.
 PATENT ASSIGNEE(S): Pennwalt Corp., USA
 SOURCE: U.S., 30 pp. Division of U.S. Ser. No. 747,151, abandoned.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-----------------------|------|----------|-----------------|----------|
| US 4210749 | A | 19800701 | US 1979-41574 | 19790521 |
| US 4233217 | A | 19801111 | US 1979-41575 | 19790521 |
| PRIORITY APPL. INFO.: | | | US 1968-711897 | 19680311 |
| | | | US 1972-241091 | 19720404 |
| | | | US 1974-523092 | 19741112 |
| | | | US 1976-747151 | 19761203 |

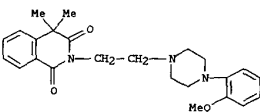
GI



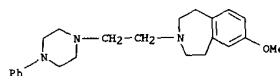
AB Benzazepines I (R = H, alkyl, alkenyl, aralkenyl, cycloalkylalkyl, aralkyl, heterocyclic alkyl) R1 = H, alkyl, Ph, phenylalkyl; R2 = H, alkyl; R3 = H, alkoxy, alkyl, halo, NO2, HO), useful as analgesics and narcotic antagonists, were prepd. Thus, treatment of 3,4-(NCCH2)2C6H3OMe with HBr-AcOH followed by heating at 85.degree. with NaOAc gave II, which was treated with BH3 to give I (R = R1 = R2 = H, R3 = MeO) (III). Refluxing III in 48% HBr gave I (R = R1 = R2 = H, R3 = HO).

IT 36134-35-7P 76216-21-2P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and pharmacol. of)
 RN 36134-35-7 CAPLUS
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

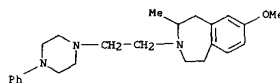
L14 ANSWER 233 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1981:44562 CAPLUS
 DOCUMENT NUMBER: 94:44562
 TITLE: Identification of .alpha.2-adrenergic receptors in human fat cell membranes by [3H]-clonidine
 binding
 AUTHOR(S): Berlan, Michel; Lafontan, Max
 CORPORATE SOURCE: Lab. Physiol. Appl. Pharmacol. Med., Fac. Med., Toulouse, F-31000, Fr.
 SOURCE: Eur. J. Pharmacol. (1980), 67(4), 481-4
 CODEN: EUPHAE; ISSN: 0014-2999
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB [3H]clonidine bound to membrane sites of human fat cells, which have the characteristics of .alpha.2-adrenoceptors. Specific binding was rapid, reversible, and saturable. [3H]clonidine binding was of high affinity with a KD of 3.9 nM and with a maximal occupancy of 348 fmol/mg protein. The correlation between .alpha.2-adrenergic agonist or antagonist affinities for the membrane [3H]clonidine binding site with their physiol. potencies demonstrates the usefulness of the human fat cell as a model for investigating postsynaptic .alpha.2-adrenoceptor properties and regulation.
 IT 67339-62-2
 RL: BIOL (Biological study) (adrenergic receptors of adipocyte cell membrane binding of, clonidine competition with)
 RN 67339-62-2 CAPLUS
 CN 1,3-(2H,4H)-isoquinolinolinedione, 2-[2-{(4-(2-methoxyphenyl)-1-piperazinyl)ethyl}-4,4-dimethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 232 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

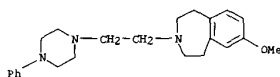


RN 76216-21-2 CAPLUS
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-8-methoxy-2-methyl-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

IT 36134-36-8P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
 RN 36134-36-8 CAPLUS
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

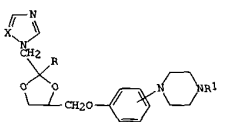


● 2 HCl

L14 ANSWER 234 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1980:620771 CAPLUS
 DOCUMENT NUMBER: 93:220771
 TITLE: Fungicidal and bactericidal[4-(piperazin-1-ylphenyloxymethyl)-1,3-dioxolan-2-ylmethyl]-1H-imidazoles and -1H-1,2,4-triazole derivatives
 INVENTOR(S): Heeres, Jan; Mostmans, Joseph
 PATENT ASSIGNEE(S): Janssen Pharmaceutica N. V., Belg.
 SOURCE: Eur. Pat. Appl., 68 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| EP 6722 | A1 | 19800109 | EP 1979-301151 | 19790615 |
| EP 6722 | B1 | 19840905 | | |
| R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE | | | | |
| AT 9227 | E | 19840915 | AT 1979-301151 | 19790615 |
| JP 63045389 | B4 | 19880909 | JP 1979-02739 | 19790702 |
| US 4503055 | A | 19850305 | US 1981-306267 | 19810928 |
| PRIORITY APPL. INFO.: | | | US 1978-921380 | 19780703 |
| | | | US 1979-23807 | 19790326 |
| | | | EP 1979-301151 | 19790615 |

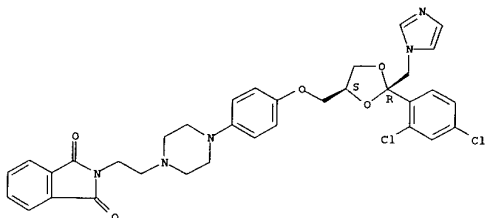
GI



AB Approx. 100 title compds. I [R = (substituted) Ph, thienyl, or halothienyl; R1 = alkylsulfonyl, CF3SO2, alkyl or alkenyl substituted by CN, (substituted) NH2, N heterocyclyl, aryl, or aryloxy, or R1 = CnH2n-1(X)R2, where R2 = H, (substituted) alkyl, alkoxy, (substituted) NH2, etc., X1 = O or S, n = 0-6; X = CH or N] were prepd. by several procedures. Thus, treatment of cis-1-[4-[(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]piperazine with ClCH2CO2Et and K2CO3 in Me2SO gave cis-I (R = 2,4-Cl2C6H3, R1 = COCH2CO2Et, X = CH), which had ED50 2.5 mg/kg (p.o) for vaginal candidosis in rats and ED50 31 mg/kg (in feed) for crop candidosis in turkeys.
 IT 75049-24-0P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and hydrolysis of)

L14 ANSWER 234 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 75049-24-0 CAPLUS
 CN 1H-Isindole-1,3(2H)-dione,
 2-[2-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-1-piperazinyl]ethyl]-, cis- (9CI) (CA INDEX NAME)

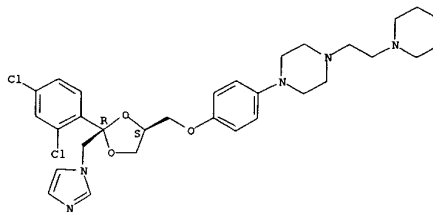
Relative stereochemistry.



IT 75049-53-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of)
 RN 75049-53-5 CAPLUS
 CN Piperazine,
 1-[4-[[2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl]methoxy]phenyl]-4-[2-(1-piperidinyl)ethyl]-, cis-, ethanedioate (1:3) (9CI) (CA INDEX NAME)
 CM 1
 CRN 75049-52-4
 CMF C31 H39 Cl2 N5 O3
 CDES 2:C15

Relative stereochemistry.

L14 ANSWER 234 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

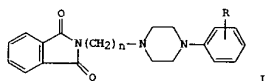


CM 2

CRN 144-62-7
 CMF C2 H2 O4



L14 ANSWER 235 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1980:550208 CAPLUS
 DOCUMENT NUMBER: 93:150208
 TITLE: Synthesis and pharmacology of N-(N4-aryl-N1-piperazinylalkyl)phthalimides: CNS depressants
 AUTHOR(S): Samant, S. D.; Kulkarni, R. A.
 CORPORATE SOURCE: Chem. Dep., Ramnarain Ruia Coll., Bombay, 400 019,
 SOURCE: India
 J. Indian Chem. Soc. (1979), 56(10), 1002-5
 CODEN: JTCSAH; ISSN: 0019-4522
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Twenty one phthalimides I (n = 1, 2, 3; R = H, Me, Cl) were prep'd. by Mannich reaction of phthalimides with piperazines in presence of HCHO or by reaction of bromoalkylphthalimides with arylpiperazines. These compds.

were inactive as central nervous system depressants. I exhibited a tranquilizing effect on test animals and were non-toxic.

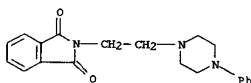
IT 75000-24-7P 75000-25-8P 75000-26-9P

75000-27-0P 75000-28-1P 75000-29-2P

75000-30-5P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and tranquilizing activity of)

RN 75000-24-7 CAPLUS

CN 1H-Isindole-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

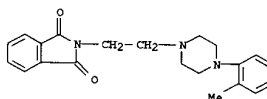


RN 75000-25-8 CAPLUS

CN 1H-Isindole-1,3(2H)-dione,

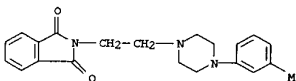
2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

L14 ANSWER 235 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



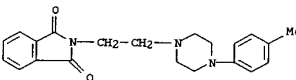
RN 75000-26-9 CAPLUS

CN 1H-Isindole-1,3(2H)-dione,
 2-[2-[4-(3-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



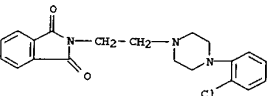
RN 75000-27-0 CAPLUS

CN 1H-Isindole-1,3(2H)-dione,
 2-[2-[4-(4-methylphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 75000-28-1 CAPLUS

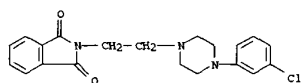
CN 1H-Isindole-1,3(2H)-dione,
 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



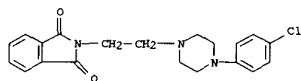
RN 75000-29-2 CAPLUS

CN 1H-Isindole-1,3(2H)-dione,
 2-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

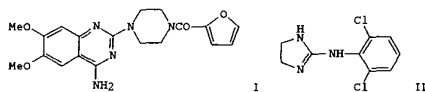
L14 ANSWER 235 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 75000-30-5 CAPLUS
CN 1H-Indole-1,3(2H)-dione,
2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-
(9CI) (CA INDEX NAME)

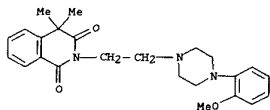


L14 ANSWER 236 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:525440 CAPLUS
DOCUMENT NUMBER: 93:125440
TITLE: 3H-Prazosin binds specifically to '.alpha.1'-
adrenoceptors in rat brain
AUTHOR(S): Miach, Peter J.; Dausse, Jean Pierre; Cardot,
Alain; Meyer, Philippe
CORPORATE SOURCE: Res. Unit, Hop. Necker, Paris, F-75015, Fr.
SOURCE: Naunyn-Schmiedeberg's Arch. Pharmacol. (1980),
312(1),
23-6
CODEN: NSAPCC; ISSN: 0028-1298
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB 3H-Labeled prazosin (I) [19216-56-9] was used to label biochem.
central .alpha.-adrenoceptors. In rat brain membranes prazosin-3H bound
specifically in a rapid, reversible and saturable manner to a single
class of high affinity sites. The relative order of potencies for
inhibition of prazosin-3H binding was WB4101 [2170-58-3] > ARC 239 [67339-62-2]
[146-48-5] which is a characteristic of the .alpha.1 type of
adrenoceptors. In contrast, the relative order of potencies for
inhibition of 3H-labeled clonidine (II) [4205-90-7] binding was
yohimbine > piperoxane > WB4101 > ARC239 > prazosin which is a characteristic
of the .alpha.2 type of adrenoceptors. Apparently, prazosin-3H binds to
central .alpha.1-receptors and clonidine-3H binds to .alpha.2-receptors
indicating the presence of two classes of .alpha.-adrenoceptors in rat brain
membranes.
IT 67339-62-2
RL: BIOL (Biological study)
(.alpha.-adrenergic receptors interaction with, in brain)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

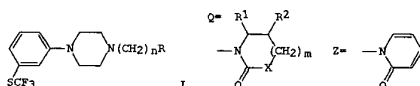
L14 ANSWER 236 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



L14 ANSWER 237 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:514564 CAPLUS
DOCUMENT NUMBER: 93:114564
TITLE: 1-Substituted
alkyl-4-(3-trifluoromethylthiophenyl)piperazines
INVENTOR(S): Najer, Henry; Manoury, Philippe; Kaplan, Jean
Pierre
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: Brit. UK Pat. Appl., 7 pp.
CODEN: BAXXDU
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

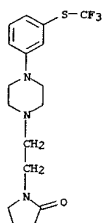
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| GB 2023594 | A | 19800103 | GB 1979-21307 | 19790619 |
| GB 2023594 | B2 | 19821013 | | |
| FR 2429216 | A1 | 19800118 | FR 1978-18352 | 19780620 |
| FR 2429216 | B1 | 19801107 | | |
| FR 2429212 | A1 | 19800118 | FR 1978-18351 | 19780620 |
| FR 2429212 | B1 | 19801107 | | |
| CA 1124238 | A1 | 19820525 | CA 1979-329703 | 19790613 |
| DK 7902510 | A | 19791221 | DK 1979-2510 | 19790615 |
| FI 7901926 | A | 19791221 | FI 1979-1926 | 19790615 |
| AU 7948112 | A1 | 19800207 | AU 1979-48112 | 19790615 |
| AU 521110 | B2 | 19820318 | | |
| US 4242343 | A | 19801230 | US 1979-48814 | 19790615 |
| NO 7902020 | A | 19791221 | NO 1979-2020 | 19790618 |
| ES 481632 | A1 | 19800216 | ES 1979-481632 | 19790618 |
| BE 877099 | A1 | 19791219 | BE 1979-195839 | 19790619 |
| SE 7905402 | A | 19791221 | SE 1979-5402 | 19790619 |
| DE 2924681 | A1 | 19800110 | DE 1979-2924681 | 19790619 |
| JP 55007274 | A2 | 19800119 | JP 1979-77489 | 19790619 |
| ZA 7903070 | A | 19800730 | ZA 1979-3070 | 19790620 |
| PRIORITY APPLN. INFO.: | | | FR 1978-18351 | 19780620 |
| | | | FR 1978-18352 | 19780620 |

GI



AB The prepn. of the title compds. I [n = 1, 2, 3; R1 = Q (R1 = R2 = H);
R1R2 = benzo; X = O, S, NH, alkylimino, CH2; m = 0, 1), Z,
2-tetrahydrofuryl,
CH2SR3 (R3 = H, alkyl, acyl), C1-8 alkoxyethyl] and I acid addn.
salts is

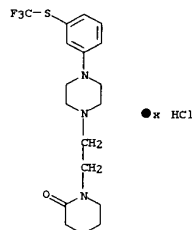
L14 ANSWER 237 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
described. Thus, I (n = 2, R = Q, R1R2 = benzo, X = NMe, m = 0) was
prepd. by heating 4-(3-trifluoromethylthiophenyl)piperazine with
powd. K2CO3, KI, and 1-(.beta.-chloroethyl)-3-methylbenzimidazolidin-2-one
in PhMe at reflux under N for 16 h. I are useful for the treatment of
anxiety and of depression. Their activity was assessed orally in
mice. LD50 values for I in mice were 75-230 mg/kg for i.p. administration
(48 h) and 250-1000 mg/kg for oral administration (7 days).
IT 74025-63-1P 74025-64-2P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as tranquilizer and antidepressant)
RN 74025-63-1 CAPLUS
CN 2-Pyrrolidinone, 1-[2-[4-[3-[(trifluoromethyl)thio]phenyl]-1-
piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



•x HCl

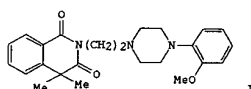
RN 74025-64-2 CAPLUS
CN 2-Piperidinone, 1-[2-[4-[3-[(trifluoromethyl)thio]phenyl]-1-
piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 237 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



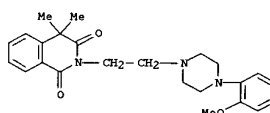
•x HCl

L14 ANSWER 238 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:437174 CAPLUS
DOCUMENT NUMBER: 93:37174
TITLE: Pharmacological properties of AR-C239,
2-[2-[4-(2-methoxyphenyl)-piperazine-1-yl]ethyl]4,4-
dimethyl-1,3(2H-4H) isoquinolinedione, a new
.alpha.-adrenoceptor blocking drug.
AUTHOR(S): Mouille, Paule; Huchet, Anne Marie; Chelly,
Jacques;
Schmitt, Lucet, Bernadette; Doursout, Marie Francoise;
Henri
CORPORATE SOURCE: Dep. Pharmacol., Fac. Med., Paris, 75270/06, Fr.
SOURCE: J. Cardiovasc. Pharmacol. (1980), 2(2), 175-91
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB In pentobarbital-treated dogs and rats, AR-C239 (I) [67339-62-2]
competitively antagonized pressor responses to adrenaline and
inhibited pressor responses to noradrenaline, phenylephrine, tyramine, and
dimethylphenylpiperazinium. Injected i.v. into closed-chest dogs,
AR-C239 (3-50 .mu.g/kg) induced a progressive fall in blood pressure, heart
rate, and sympathetic nerve activity. The drug appears to be devoid of
direct vasodilator action, and the fall in blood pressure results from the
peripheral .alpha.-blockade. AR-C239 did not change the tachycardia
induced by stimulation of the cardiac nerve in dogs and, at least in
this prepn., seems to be a specific .alpha.1-adrenoceptor blocking drug.
When administered into the cisterna magna of dogs, AR-C239 did not have
any centrally mediated cardiovascular actions and failed to block the
inhibitor effects of clonidine on blood pressure and heart rate.
AR-C239 did not have any centrally mediated cardiovascular actions and
failed to block the inhibitory effects of clonidine on blood pressure and heart
rate. AR-C239 did not modify the functioning of the baroreflex arc.
Due

L14 ANSWER 238 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
to its specificity for .alpha.1-adrenoceptors, AR-C239 may be useful
for characterizing .alpha.-adrenoceptors.
IT 67339-62-2
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. of)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-
piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

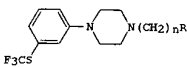


L14 ANSWER 239 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:426462 CAPLUS
DOCUMENT NUMBER: 93:26462
TITLE: Phenylpiperazine derivatives
PATENT ASSIGNEE(S): Synthelabo S. A., Fr.
SOURCE: Meth. Appl., 9 pp.
CODEN: NAXXAN
DOCUMENT TYPE: Patent
LANGUAGE: Dutch
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| NL 7904755 | A | 19791227 | NL 1979-4755 | 19790619 |
| FR 2429216 | A1 | 19800118 | FR 1978-18352 | 19780620 |
| FR 2429216 | B1 | 19801107 | | |
| FR 2429212 | A1 | 19800118 | FR 1978-18351 | 19780620 |
| FR 2429212 | B1 | 19801107 | | |
| CA 1124238 | A1 | 19820525 | CA 1979-329703 | 19790613 |
| DK 7902510 | A | 19791221 | DK 1979-2510 | 19790615 |
| FI 7901926 | A | 19791221 | FI 1979-1926 | 19790615 |
| AU 7948112 | A1 | 19800207 | AU 1979-48112 | 19790615 |
| AU 521110 | B2 | 19820318 | | |
| US 4242343 | A | 19801230 | US 1979-48814 | 19790615 |
| NO 7902020 | A | 19791221 | NO 1979-2020 | 19790618 |
| ES 481632 | A1 | 19800216 | ES 1979-481632 | 19790618 |
| BE 577099 | A1 | 19791219 | BE 1979-195839 | 19790619 |
| SE 7905402 | A | 19791221 | SE 1979-5402 | 19790619 |
| DE 2924681 | A1 | 19800110 | DE 1979-2924681 | 19790619 |
| JP 55007274 | A2 | 19800119 | JP 1979-77489 | 19790619 |
| ZA 7903070 | A | 19800730 | ZA 1979-3070 | 19790620 |

PRIORITY APPLN. INFO.: FR 1978-18351 19780620
FR 1978-18352 19780620

GI

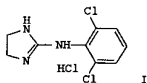


AB Tranquilizing (no data) piperazines I (n = 1-3; R = heterocyclic amino) were prepd. Thus, 4-(3-trifluoromethylthiophenyl)piperazine was treated with 1-(2-chloroethyl)-2-pyridone to give I (n = 2, R = 2-oxo-1-pyridyl).

IT 74025-63-1P 74025-64-2P
RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

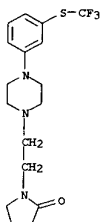
RN 74025-63-1 CAPLUS
CN 2-Pyrrolidinone, 1-[2-[4-[3-[(trifluoromethyl)thio]phenyl]-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 240 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1980:174421 CAPLUS
DOCUMENT NUMBER: 92:174421
TITLE: Interactions between clonidine and .alpha.-adrenoceptor blocking drugs on the tachycardic response to stimulation of the cardiac nerve in dogs
AUTHOR(S): Mouille, Paule; Huchet, Anne Marie; Lucet, Bernadette;
CORPORATE SOURCE: Chelly, Jacques; Schmitt, Henri
SOURCE: Dep. Pharm., Fac. Med. Broussais, Paris, Fr. J. Cardiovasc. Pharmacol. (1979), 1(5), 515-28
CODEN: JCPCTD; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



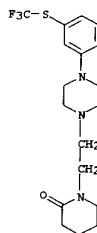
AB In pentobarbital-treated dogs clonidine-HCl (I) [4205-91-8] (10 .mu.g/kg) reduced the increase in heart rate caused by elec. stimulation of the cardiac nerve (1-10 Hz). Yohimbine-HCl [65-19-0] (0.3 mg/kg) and phentolamine-HCl [73-05-2] (1 mg/kg) potentiated the effects of nerve stimulation and antagonized the inhibitory effects of I. Piperoxan-HCl [135-97-5] (1 mg/kg) increased the response to nerve stimulation but antagonized the effects of I only at the lowest frequency of stimulation. Thymoxamine-HCl [964-52-3] (1 mg/kg) and prazosin-HCl [19237-84-4] at high doses (1 mg/kg) also antagonized the effects of I but failed to increase the pos. chronotropic response to stimulation of the cardiac nerve. AR-C239 [67339-62-2], a new and potent .alpha.-adrenoceptor blocking agent, changed neither the response to nerve stimulation nor the inhibitory effect of I. The effects of all these drugs were obsd. at doses which reduced or reversed the pressor response to adrenaline. Therefore, the results afford further evidence for a dissimilarity between postsynaptic and presynaptic .alpha.-adrenoceptors in the dog. In addn., they show that the failure of an .alpha.-adrenoceptor blocking compd. to increase the response to nerve stimulation does not necessarily indicate a lack of presynaptic .alpha.-adrenoceptor blockade.

L14 ANSWER 239 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



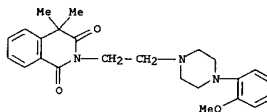
●x HCl

RN 74025-64-2 CAPLUS
CN 2-Piperidinone, 1-[2-[4-[3-[(trifluoromethyl)thio]phenyl]-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

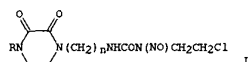


●x HCl

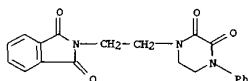
L14 ANSWER 240 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
IT 67339-62-2
RL: BIOL (Biological study) (heart response to clonidine in relation to)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



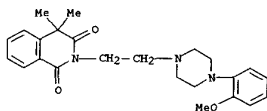
L14 ANSWER 241 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1979:611367 CAPLUS
 DOCUMENT NUMBER: 91:211367
 TITLE: Synthesis and physico-chemical properties of 1-(2-chloroethyl)-3-(4-substituted-2,3-dioxo-1-piperazinylalkyl)-1-nitrosourea
 AUTHOR(S): Yoshida, Hori, Takako; Momono, Kaishu; Kiba, Yasuo; Chosaku Sakai, Hiroshi; Takeno, Ryuko; Ohashi, Toshinori; Kishimoto, Sumiko; Saikawa, Isamu Res. Lab., Toyama Chem. Co., Ltd., Toyama, Japan
 CORPORATE SOURCE: Yakuaku Zasshi (1979), 99(7), 730-7
 SOURCE: CODEN: YKKZAJ; ISSN: 0031-6903
 DOCUMENT TYPE: Journal
 LANGUAGE: Japanese
 GI



AB 1-(2-Chloroethyl)-3-(4-substituted-2,3-dioxo-1-piperazinylalkyl)-1-nitrosourea I (R = H, Cl-8 alkyl, Ph; n = 0-6) were prepd. by treating the dioxopiperazinylalkylamines with 4-O2NC6H4O2CN(NO)CH2CH2Cl on with ClCH2CH2NCO followed by nitrosation and their physico-chem. properties were examd. Along with an increase in n, the alkylating activity was reduced, the stability in aq. soln. at pH 7-8 was increased, and the NH proton of the NMR spectrum was shifted to a higher field. These properties were not related to R.
 IT 71999-88-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and hydrazinolysis of)
 RN 71999-88-7 CAPLUS
 CN 1H-isoindole-1,3(2H)-dione, 2-[2-(2,3-dioxo-4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 242 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

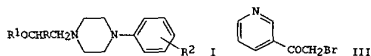


L14 ANSWER 242 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1979:115517 CAPLUS
 DOCUMENT NUMBER: 90:115517
 TITLE: Biochemical evidence for presynaptic and postsynaptic .alpha.-adrenoceptors in rat heart membranes: Positive homotropic cooperativity of presynaptic binding
 AUTHOR(S): Guicheney, Pascale; Garay, Ricardo P.; Levy-Marchal, Claire; Meyer, Philippe
 CORPORATE SOURCE: Dep. Physiol. Pharmacol., Hop. Necker, Paris, Fr.
 SOURCE: Proc. Natl. Acad. Sci. U. S. A. (1978), 75(12), 6285-9
 CODEN: PNASA6; ISSN: 0027-8424
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB In crude rat cardiac membrane prepsn., dihydroergocryptine-3H (I) appeared to bind 2 classes of sites with limited capacity, differing in their specificities and their affinities. The 1st class of binding sites interacted preferentially with the postsynaptic .alpha.-adrenoceptor blocker ARC 239 [67339-62-2], as expected for postsynaptic .alpha.-adrenoceptors. The binding of I to these receptors followed the law of mass action, with a high affinity for I apparent dissociation constant (Kd) at 25.degree. = 1.67 nM. Postsynaptic satg. levels of I were necessary to occupy the 2nd class of binding sites. These sites exhibit a preferential affinity for presynaptic ligands such as clonidine [4205-90-7] and yohimbine-HCl [65-19-0], as expected for presynaptic .alpha.-adrenergic receptors. This presynaptic binding showed a markedly pos. homotropic cooperativity (Hill n = 2.88) with initial and final Kds of 23 and 0.83 nM, resp. Free energy of interaction between sites was of the order of 2 kcal (8.36 kJ)/mol of sites. These characteristics provide a rational mol. basis for the functional role of presynaptic .alpha.-adrenoceptors that mediate the inhibition of norepinephrine release from nerve endings.
 IT 67339-62-2
 RL: PROC (Process) (heart membrane binding of)
 RN 67339-62-2 CAPLUS
 CN 1,3(2H,4H)-isoquinolinadione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)

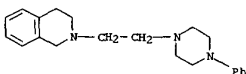
L14 ANSWER 243 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1978:597598 CAPLUS
 DOCUMENT NUMBER: 89:197598
 TITLE: 1-Alkyl-substituted 4-phenylpiperazine derivatives
 PATENT ASSIGNEE(S): MALESCI S.a.S. Istituto Farmacobiologico, Italy
 SOURCE: Span., 29 pp.
 CODEN: SPXXAD
 DOCUMENT TYPE: Patent
 LANGUAGE: Spanish
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| ES 452530 | A3 | 19780201 | ES 1976-452530 | 19761019 |

GI

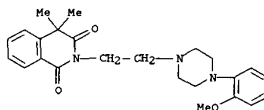


AB 1-Alkyl-4-aryl-piperazines I (R = pyridyl, 4-imidazolyl, 1,2,3,4-tetrahydro-2-isoquinolyl, 1,2,3,4-tetrahydro-2-methyl-3-isoquinolyl; R1 = alkyl, R2 = H, Cl, F, Me, MeO) were prepd. by treatment of ROCH2Br with 1-phenylpiperazine (II) or its aryl-substituted derivs., followed by redn. with NaBH4 and O-alkylation. Thus, III.HBr was treated with II in MeOH-Et3N under N at 5-10.degree. and then at room temp. The mixt. was cooled to 0.degree., aq. NaBH4 added dropwise and the mixt. kept at room temp. for 1 h. The product (I; R = 3-pyridyl, R1 = R2 = H) in HCCl3 at 0.degree. was treated with HCl (g), SOCl2 in HCCl3, and MeOH to give I (R = 3-pyridyl, R1 = Me, R2 = H).
 IT 58013-22-2P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
 RN 58013-22-2 CAPLUS
 CN Isoquinoline, 1,2,3,4-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

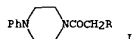


L14 ANSWER 243 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

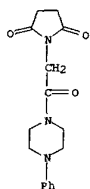
L14 ANSWER 244 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:500074 CAPLUS
DOCUMENT NUMBER: 89:100074
TITLE: Modifications of effects of cardiovascular nerve stimulation in the dog, by clonidine and several .alpha.-adrenolytics
AUTHOR(S): Mouille, Paule; Buchet, Anne-Marie; Lucet, Bernadette;
CORPORATE SOURCE: Schmitt, Henri
SOURCE: Fac. med., Paris-Broussais-Hotel-Dieu, Paris, Fr. C. R. Hebd. Seances Acad. Sci., Ser. D (1978), 286(19), 1399-402
CODEN: CHDDAT; ISSN: 0567-655X
DOCUMENT TYPE: Journal
LANGUAGE: French
AB In anesthetized dogs clonidine [4205-90-7] (0.01mg/kg, i. v.) reduced the tachycardia induced by stimulation of the cardiac nerve at low frequencies. Small doses of yohimbine [146-48-5] (0.3mg/kg, i. v.) or piperoxan [59-39-2] (0.3 mg/kg, i. v.) increased the effects of nerve stimulation and in addn. antagonized the inhibitory effects of clonidine and reversed the pressor response to adrenaline [51-43-4].
Thymoxamine [54-32-0] (1 mg/kg, i. v.) and prazosin [19216-56-9] (1 mg/kg, i. v.) did not increase the effect of cardiac nerve stimulation, but reduced the effect of clonidine. ARC239 [67339-62-2] (0.05mg.kg-1) reversed the pressor response to adrenaline but even at high doses did not increase the effects of cardiac nerve stimulation or the effects of clonidine. Thus, pre- and post-synaptic .alpha.-adrenoceptors appear to be dissimilar.
IT 67339-62-2
RL: BIOL (Biological study)
in (tachycardia from cardiac nerve stimulation response to, quantity relation to)
RN 67339-62-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl- (9CI) (CA INDEX NAME)



L14 ANSWER 245 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1978:50793 CAPLUS
DOCUMENT NUMBER: 88:50793
TITLE: Investigations on the piperazine series. New N-phenyl-piperazine acylate derivatives
AUTHOR(S): Zotta, V.; Popescu, Margareta; Missir, A.; Soare, Jeana; Capitanescu, Victoria; Predescu, Viorica;
Dicu,
CORPORATE SOURCE: Elena; Neacsu, Maria
SOURCE: Lab. Chim. Farm., Fac. Farm., Bucharest, Rom. Farmacia (Bucharest) (1977), 25(3), 129-35
CODEN: FRMBAZ
DOCUMENT TYPE: Journal
LANGUAGE: Romanian
GI

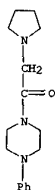


AB Nine piperazines I (R = 2,5-dioxopiperidino, piperidino, pyrrolidino, 2-pyridylamino, morpholino, etc.) were prepd. by treating I (R = Cl) with amines.
IT 65349-00-0P 65349-01-1P 65349-02-2P
RL: SYN (Synthetic preparation); PREP (Preparation) (prepn. of)
RN 65349-00-0 CAPLUS
CN Piperazine, 1-[(2,5-dioxo-1-pyrrolidinyl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)

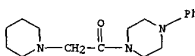


RN 65349-01-1 CAPLUS
CN Piperazine, 1-phenyl-4-(1-pyrrolidinylacetyl)- (9CI) (CA INDEX NAME)

L14 ANSWER 245 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

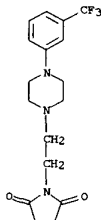


RN 65349-02-2 CAPLUS
CN Piperazine, 1-phenyl-4-(1-piperidinylacetyl)- (9CI) (CA INDEX NAME)



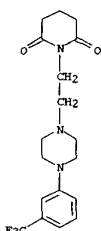
L14 ANSWER 246 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1977:495439 CAPLUS
 DOCUMENT NUMBER: 87:95439
 TITLE: Substituted trifluoromethyl phenyl piperazines as anorectic agents
 AUTHOR(S): Cross, Peter E.; Dickinson, Roger P.; Halliwell, Geoffrey; Kemp, John E. G.
 CORPORATE SOURCE: Pfizer Cent. Res., Pfizer Ltd., Sandwich/Kent, Engl.
 SOURCE: Eur. J. Med. Chem. - Chim. Ther. (1977), 12(2), 173-6
 CODEN: EJMCAS
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI For diagram(s), see printed CA Issue.
 AB In a series of trifluoromethyl phenyl piperazines possessing cyclo-imido alkyl side chains (I) several compds. possessed good anorectic activity with min. side effects on the central nervous system. The most potent no. of the series was 1-(2-succinimidoethyl)-4-[4'-chloro-3-trifluoromethylphenyl]piperazine-HCl (II) [41213-05-2], which was prepd. by heating 1-[4'-chloro-3-(trifluoromethyl)phenyl]piperazine-HCl [63556-37-6] with 2-succinimidoethyl chloride [41212-96-8] in dry dimethylformamide in the presence of base.
 IT 41212-97-9P 41212-99-1P 41213-05-2P 63556-31-0P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. and anorectic activity of)
 RN 41212-97-9 CAPLUS
 CN 2,5-Pyrrolidinedione, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 246 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

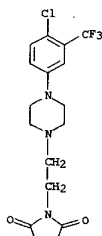
RN 41212-99-1 CAPLUS
 CN 2,6-Piperidinedione, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

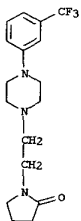
RN 41213-05-2 CAPLUS
 CN 2,5-Pyrrolidinedione, 1-[2-[4-[4-chloro-3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 246 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



● HCl

RN 63556-31-0 CAPLUS
 CN 2-Pyrrolidinone, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

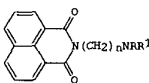


● HCl

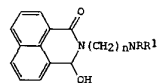
L14 ANSWER 247 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1977:171284 CAPLUS
 DOCUMENT NUMBER: 86:171284
 TITLE: 2-[(Piperidinyl or tetrahydropyridinyl)-alkyl]-2,3-dihydro-3-hydroxy-1H-benz[de]isoquinolin-1-ones
 INVENTOR(S): Wade, Peter C.; Vogt, Berthold Richard
 PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc., USA
 SOURCE: U.S., 18 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| US 4007191 | A | 19770208 | US 1975-621939 | 19751014 |
| GB 1567313 | A | 19800514 | GB 1976-41959 | 19761008 |
| CA 1068703 | A1 | 19791224 | CA 1976-263130 | 19761012 |
| JP 52048674 | A2 | 19770418 | JP 1976-123369 | 19761014 |
| DE 2646471 | A1 | 19770421 | DE 1976-2646471 | 19761014 |
| FR 2327782 | A1 | 19770513 | FR 1976-30936 | 19761014 |
| FR 2327782 | B1 | 19781222 | | |

PRIORITY APPLN. INFO.: US 1975-621939 19751014
 GI

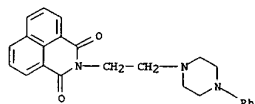


I



II

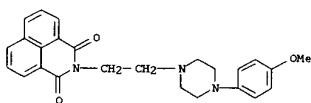
AB Benzisoquinolinediones I (n = 2-6, NRR1 = 4-substituted 1,2,3,6-tetrahydropyridino, piperidino, piperazino) were prepd. by treating naphthalic anhydride with H2N(CH2)nOH, tosylating, and treating the ester with HNRR1 or by treating naphthalimide with Br(CH2)nBr and HNRR1. I were reduced with NaBH4 to give II which have antidepressant activity (no data).
 IT 58895-65-1P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. and redn. of)
 RN 58895-65-1 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

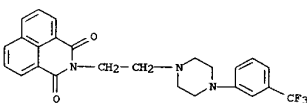
IT 58895-66-2P 58895-67-3P 58895-68-4P
 58895-69-5P 58895-70-8P 58895-71-9P
 58895-76-4P 58895-78-6P 62614-87-3P
 RL: SPN (Synthetic Preparation); PREP (Preparation)
 (prepn. of)

RN 58895-66-2 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-(4-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



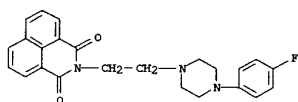
● 2 HCl

RN 58895-67-3 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



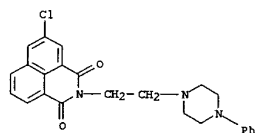
● HCl

RN 58895-71-9 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-(4-fluorophenyl)-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



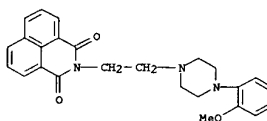
● HCl

RN 58895-76-4 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 5-chloro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



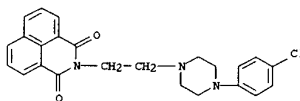
● HCl

RN 58895-78-6 CAPLUS



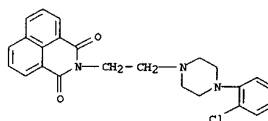
● 2 HCl

RN 58895-68-4 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-(4-chlorophenyl)-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

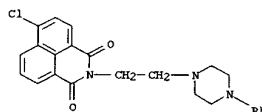


● HCl

RN 58895-69-5 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-(2-chlorophenyl)-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

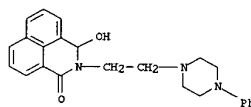


RN 58895-70-8 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-[3-(trifluoromethyl)phenyl]-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 62614-87-3 CAPLUS
 CN 1H-Benz[de]isoquinolin-1-one, 2,3-dihydro-3-hydroxy-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

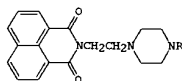


L14 ANSWER 248 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1976:150664 CAPLUS
 DOCUMENT NUMBER: 84:150664
 TITLE: 2-[(Substituted-piperazinyl)alkyl]-1H-benz[de]isoquinoline-1,3(2H)-diones
 INVENTOR(S): Wade, Peter C.; Vogt, Berthold R.
 PATENT ASSIGNEE(S): Squibb, E. R., and Sons, Inc., USA
 SOURCE: U.S., 8 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| US 3940397 | A | 19760224 | US 1974-523293 | 19741113 |
| CA 1058178 | A1 | 19790710 | CA 1975-239072 | 19751105 |
| DE 2551062 | A1 | 19760526 | DE 1975-2551062 | 19751113 |
| FR 2290903 | A1 | 19760611 | FR 1975-34615 | 19751113 |
| FR 2290903 | B1 | 19781110 | | |
| JP 51125293 | A2 | 19761101 | JP 1975-137115 | 19751113 |

PRIORITY APPLN. INFO.:
 US 1974-523293 19741113
 US 1975-543558 19750123

GI



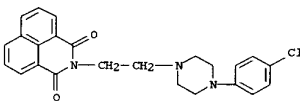
1

AB Benzoisoquinolinediones (I, R = Ph, p-MeO-, o-MeOC6H4, p-Cl-, o-ClC6H4, m-F3CC6H4, p-FC6H4, PhCH2) were obtained as their hydrochlorides by treatment of naphthalic anhydride with H2NCH2CH2OH to give a hydroxyethylbenzoisoquinolinedione which was treated with p-MeOC6H4-SO2Cl to give a sulfonate ester followed by treatment with the corresponding piperazine deriv. I were useful as antidepressants and inflammation inhibitors.

IT 58895-65-1P 58895-66-2P 58895-67-3P
 58895-68-4P 58895-69-5P 58895-70-8P
 58895-71-9P 58895-76-4P 58895-78-6P
 RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)

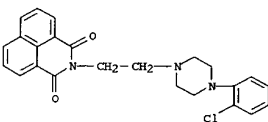
RN 58895-65-1 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 248 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
 piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

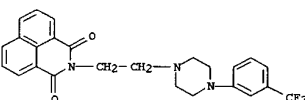


● HCl

RN 58895-69-5 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



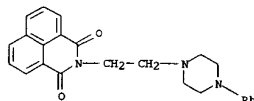
RN 58895-70-8 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

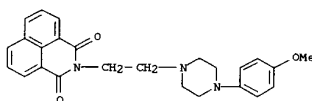
RN 58895-71-9 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-fluorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 248 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



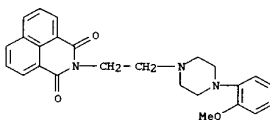
● 2 HCl

RN 58895-66-2 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

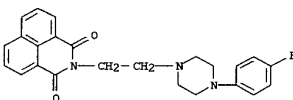
RN 58895-67-3 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



● 2 HCl

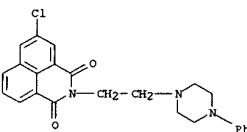
RN 58895-68-4 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 2-[2-[4-(4-chlorophenyl)-1-

L14 ANSWER 248 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



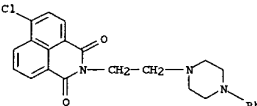
● HCl

RN 58895-76-4 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 5-chloro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

RN 58895-78-6 CAPLUS
 CN 1H-Benz[de]isoquinoline-1,3(2H)-dione, 6-chloro-2-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

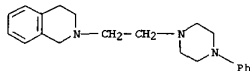


● HCl

L14 ANSWER 249 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1976:59553 CAPLUS
 DOCUMENT NUMBER: 84:59553
 TITLE: Heterocyclic derivatives of substituted
 1-alkyl-4-phenylpiperazine
 INVENTOR(S): Giannini, Mario
 PATENT ASSIGNEE(S): MAJESCI S.a.S. Istituto Farmacobiologico, Italy
 SOURCE: Belg., 31 pp.
 CODEN: BEKKAL
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| BE 820242 | A2 | 19750116 | BE 1974-2053876 | 19740924 |
| CH 624402 | A | 19810731 | CH 1974-11406 | 19740821 |
| | | | IT 1974-48923 | 19740301 |

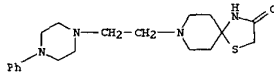
PRIORITY APPLN. INFO.:
 G1 For diagram(s), see printed CA Issue.
 AB Antihypertensive (no data) piperazines I were prepd. Thus, I (R = 4-imidazolyl, R1 = H, R2 = H, 2-Me, 4-Me, 2-Cl, 2-OMe, 4-Cl, 4-OMe, n = 0; R = 2-pyridyl (py), 3-py, 4-py, R1 = R2 = H, n = 0; R = 3-py, R1 = H, R2 = H, 2-OMe, 2-Cl, n = 1; R = 3-py, R1 = R2 = H, n = 2; R = 1,2,3,4-tetrahydro-2-isoquinolyl, R1 = R2 = H, n = 1; R = 2-methyl-1,2,3,4-tetrahydro-3-isoquinolyl, R1 = R2 = H, n = 0) were prepd. by treating N-arylpiperazines (II) with R(CH2)n+1Cl. I (R = 3-py, R1 = OH, R2 = H, 2-OMe, 3-OMe, 4-OMe, 2-Me, 3-Me, 4-Me, 2-Cl, 3-Cl, 4-Cl, n = 1; R = 4-py, R1 = OH, R2 = H, 2-OMe, n = 1) were prepd. by treating II with RCOCH2Br and reducing the ketone in situ with NaBH4. I (R = 3-py, R1 = OMe, OEt, R2 = H, 2-OMe, 2-Cl, n = 1) were obtained by alkylating I (R1 = OH).
 IT 58013-22-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (Prepn. of)
 RN 58013-22-2 CAPLUS
 CN Isoquinoline, 1,2,3,4-tetrahydro-2-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 250 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1976:44001 CAPLUS
 DOCUMENT NUMBER: 84:44001
 TITLE: Spirocyclic compounds
 INVENTOR(S): Nakanishi, Michio; Arimura, Katsuo; Tsing, In Mu
 PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd., Japan
 SOURCE: Japan., 4 pp.
 CODEN: JAKKAD
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 49028195 | B4 | 19740724 | JP 1970-4618 | 19700117 |

G1 For diagram(s), see printed CA Issue.
 AB Twenty-six thiazaspiro compds. (I, n = 2, 3, R = Me, m-ClC6H4, p-ClC6H4, etc., R1 = Me2N, Et2N, morpholino, H2N, 3-piperidinyl etc.,) or their hydrochlorides or maleates, useful as antispasmodics, analgesics, and sedatives, (no data) were prepd. by reacting the appropriate 1-(aminoalkyl)-4-piperidinone with HSCH2CO2H and (NH4)2CO3 (for I where R1 = H2N) or with RH. E.g., 18.4 g 1-[3-(dimethylamino)propyl]-4-oxopiperidine was refluxed with 14.5 g (NH4)2CO3 and 11 g HSCH2CO2H in 400 ml benzene for 15 hr to give 14 g I (n = 3, R = H, R1 = Me2N).contdot.2HCl.
 II was prepd. similarly.
 IT 54950-45-7P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (Prepn. of)
 RN 54950-45-7 CAPLUS
 CN 1-Thia-4,8-diazaspiro[4.5]decan-3-one, 8-[2-(4-phenyl-1-piperazinyl)ethyl]-, (2Z)-2-butenedioate (1:2) (9CI) (CA INDEX NAME)
 CH 1
 CRN 54950-44-6
 CHF C19 H28 N4 O S



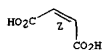
CH 2

CRN 110-16-7

L14 ANSWER 250 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

CMF C4 H4 O4
CDES 2:2

Double bond geometry as shown.



L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1975:443207 CAPLUS
DOCUMENT NUMBER: 83:43207
TITLE: 2-(Piperazinylalkyl)isoquinolinediones
INVENTOR(S): Kutter, Eberhard; Austel, Volkhard; Eberlien, Wolfgang; Heider, Joachim
PATENT ASSIGNEE(S): thomae, Ger.
SOURCE: Ger. Offen., 23 pp.
CODEN: GWXXRX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| DE 2345422 | A1 | 19750320 | DE 1973-2345422 | 19730908 |
| DE 2345422 | C2 | 19831222 | | |
| AT 7406514 | A | 19751015 | AT 1974-6514 | 19740808 |
| AT 330777 | B | 19760726 | | |
| FI 7402465 | A | 19750309 | FI 1974-2465 | 19740821 |
| FI 52219 | B | 19770331 | | |
| ES 429473 | A1 | 19760901 | ES 1974-429473 | 19740823 |
| US 3948898 | A | 19760406 | US 1974-503072 | 19740904 |
| SU 528035 | D | 19760905 | SU 1974-2057995 | 19740904 |
| AU 7473023 | A1 | 19760311 | AU 1974-73023 | 19740905 |
| BE 819651 | A1 | 19750306 | BE 1974-148302 | 19740906 |
| SE 7411312 | A | 19750310 | SE 1974-11312 | 19740906 |
| SE 424863 | B | 19820816 | | |
| SE 424863 | C | 19821125 | | |
| NO 7403220 | A | 19750311 | NO 1974-3220 | 19740906 |
| NO 140978 | B | 19790910 | | |
| NL 7411843 | A | 19750311 | NL 1974-11843 | 19740906 |
| NL 176363 | B | 19841101 | | |
| NL 176363 | C | 19850401 | | |
| FR 2242979 | A1 | 19750404 | FR 1974-30387 | 19740906 |
| DK 7404727 | A | 19750505 | DK 1974-4727 | 19740906 |
| JP 50050381 | A2 | 19750506 | JP 1974-102862 | 19740906 |
| JP 59006868 | B4 | 19840215 | | |
| DD 115122 | C | 19750912 | DD 1974-180966 | 19740906 |
| HU 167869 | F | 19751225 | HU 1974-70980 | 19740906 |
| ZA 7405688 | A | 19760526 | ZA 1974-5688 | 19740906 |
| GB 1446791 | A | 19760818 | GB 1974-39083 | 19740906 |
| CH 605778 | A | 19781013 | CH 1974-12189 | 19740906 |
| CH 605779 | A | 19781013 | CH 1977-16014 | 19740906 |
| RO 63655 | F | 19781015 | RO 1974-79932 | 19740906 |
| CS 185660 | P | 19781031 | CS 1974-6150 | 19740906 |
| PL 91712 | P | 19770331 | PL 1974-173958 | 19740907 |
| ES 433959 | A1 | 19761116 | ES 1975-433959 | 19750120 |
| ES 433958 | A1 | 19761116 | ES 1975-433958 | 19750120 |
| SU 538664 | D | 19761205 | SU 1975-2145942 | 19750620 |
| SU 545256 | D | 19770130 | SU 1975-2145935 | 19750620 |
| AT 7505607 | A | 19760515 | AT 1975-5607 | 19750721 |
| AT 334375 | B | 19760110 | | |
| AT 7505606 | A | 19760515 | AT 1975-5606 | 19750721 |
| AT 334374 | B | 19760110 | | |
| US 4021558 | A | 19770503 | US 1976-651568 | 19760122 |

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

PRIORITY APPLN. INFO.:

DE 1973-2345422 19730908
DE 1973-2345423 19730908
AT 1974-6514 19740808
US 1974-503072 19740904

G1 For diagram(s), see printed CA issue.

AB Twenty-five isoquinolinediones I (R = Ph, substituted Ph, or 2-pyridyl; R1

= H or Me; R2 = H, F, Cl, or MeO; n = 2 or 3), useful as

antihypertensives or sedatives or in tachycardia treatment (no data), were prep'd. by

reaction of the isochromandiones (II, X = O) or isoquinolinediones

II (X = NH) with (1-piperazinyl)alkylamines or (1-piperazinyl)alkyl

chlorides, resp., or by reaction of the isoquinolinediones [11, X = N(CH₂)nCl]

with the piperazines.

IT 55974-36-2P 55974-37-3P 55974-38-4P

55974-39-5P 55974-40-8P 55974-42-0P

55974-43-1P 55974-45-3P 55974-46-4P

55974-47-5P 55974-48-6P 55974-49-7P

55974-51-1P 55974-52-2P 56010-74-3P

56045-26-2P

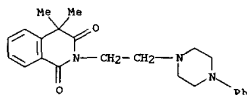
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of antihypertensive and sedative)

RN 55974-36-2 CAPLUS

CN 1,3(2H,4H)-isoquinolinedione, 4,4-dimethyl-2-[2-(4-phenyl-1-

piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



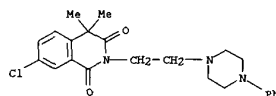
● 2 HCl

RN 55974-37-3 CAPLUS

CN 1,3(2H,4H)-isoquinolinedione, 7-chloro-4,4-dimethyl-2-[2-(4-phenyl-1-

piperazinyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

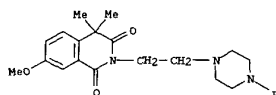


● x HCl

RN 55974-38-4 CAPLUS

CN 1,3(2H,4H)-isoquinolinedione, 7-methoxy-4,4-dimethyl-2-[2-(4-phenyl-1-

piperazinyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)

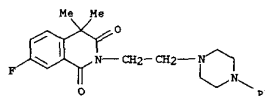


● x HCl

RN 55974-39-5 CAPLUS

CN 1,3(2H,4H)-isoquinolinedione, 7-fluoro-4,4-diphenyl-2-[2-(4-phenyl-1-

piperazinyl)ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



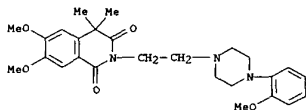
● x HCl

RN 55974-40-8 CAPLUS

CN 1,3(2H,4H)-isoquinolinedione, 6,7-dimethoxy-2-[2-(4-(2-methoxyphenyl)-1-

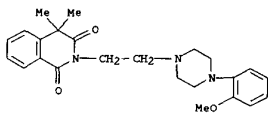
piperazinyl)ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



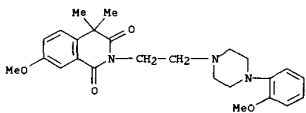
●x HCl

RN 55974-42-0 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 55974-43-1 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 7-methoxy-2-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

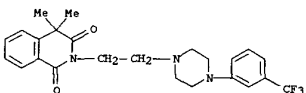


●2 HCl

RN 55974-45-3 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-(3-methyl-4-phenyl-1-

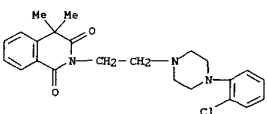
L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)

RN 55974-48-6 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

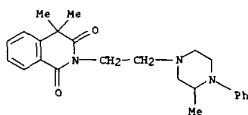
RN 55974-49-7 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

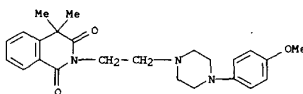
RN 55974-51-1 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-[3,4-dimethoxyphenyl]-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



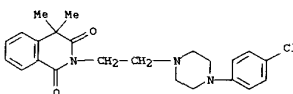
●2 HCl

RN 55974-46-4 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



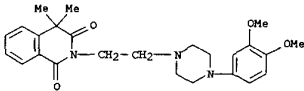
●2 HCl

RN 55974-47-5 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(4-chlorophenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



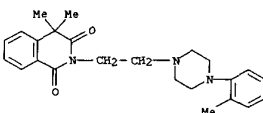
●2 HCl

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



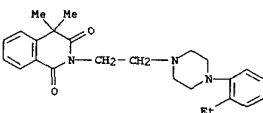
●2 HCl

RN 55974-52-2 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 4,4-dimethyl-2-[2-[4-(2-methylphenyl)-1-piperazinyl]ethyl]-, hydrochloride (9CI) (CA INDEX NAME)



●x HCl

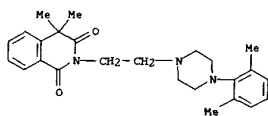
RN 56010-74-3 CAPLUS
CN 1,3(2H,4H)-Isoquinolinedione, 2-[2-[4-(2-ethylphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

RN 56045-26-2 CAPLUS

L14 ANSWER 251 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)



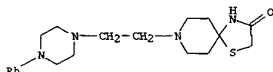
●X HCl

L14 ANSWER 252 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
CN 1,3(2H,4H)-isoquinolinedione, 2-[2-[4-(2,6-dimethylphenyl)-1-piperazinyl]ethyl]-4,4-dimethyl-, hydrochloride (9CI) (CA INDEX NAME)

CH 1

CRN 54950-44-6

CMF C19 H28 N4 O S



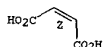
CH 2

CRN 110-16-7

CMF C4 H4 O4

CDES 2:2

Double bond geometry as shown.

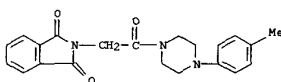


L14 ANSWER 252 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1975:410049 CAPLUS
DOCUMENT NUMBER: 83:10049
TITLE: Spirocyclic compounds
INVENTOR(S): Arimura, Katsuo; Kohayagawa, Takahiro; Tsing, In Mu;
PATENT ASSIGNEE(S): Tsuda, Yoshiaki
SOURCE: Yoshitomi Pharmaceutical Industries, Ltd.
CODEN: JAXKAD
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

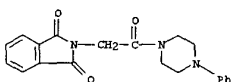
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 49029196 | B4 | 19740801 | JP 1971-48716 | 19710702 |
| CH 501635 | A | 19710115 | CH 1968-501635 | 19680229 |
| NL 6902779 | A | 19690902 | NL 1969-2779 | 19690221 |
| DK 122725 | B | 19720404 | DK 1969-982 | 19690221 |
| US 3624075 | A | 19711130 | US 1969-801801 | 19690224 |
| FR 2002897 | A5 | 19691031 | FR 1969-5170 | 19690227 |
| BE 729209 | A | 19690828 | BE 1969-729209 | 19690228 |
| AT 286994 | B | 19710111 | AT 1969-2038 | 19690228 |
| AT 286997 | B | 19710111 | AT 1970-2017 | 19690228 |
| AT 286996 | B | 19710111 | AT 1970-2014 | 19690228 |
| ES 364635 | A1 | 19710201 | ES 1969-364635 | 19690228 |
| ES 364633 | A1 | 19710201 | ES 1969-364633 | 19690228 |
| ES 364637 | A1 | 19710201 | ES 1969-364637 | 19690228 |
| ES 364634 | A1 | 19710201 | ES 1969-364634 | 19690228 |
| ES 364632 | A1 | 19710201 | ES 1969-364632 | 19690228 |
| AT 287729 | B | 19710210 | AT 1970-2015 | 19690228 |
| AT 289815 | B | 19710510 | AT 1970-2016 | 19690228 |
| GB 1259648 | A | 19720105 | GB 1969-1259648 | 19690228 |
| BR 6906750 | A0 | 19730419 | BR 1969-206750 | 19690228 |
| JP 49027876 | B4 | 19740722 | JP 1969-14996 | 19690228 |
| JP 49029197 | B4 | 19740801 | JP 1971-48717 | 19710702 |

PRIORITY APPLN. INFO.: CH 1968-3055 19680229
GI For diagram(s), see printed CA Issue.
AB Forty-three I [(R = Me2NCH2CH2, Me2N(CH2)3, Et2N(CH2)2, Et2N(CH2)3, 2-piperidinoethyl, 3-morpholinopropyl, etc.; R1 = H, Me; R2 = Ph, H, Et, C6H4CF3-m, C6H4Cl-p, etc.) or their salts, useful as analgesics and tranquilizers (no data), were prepd. from RX (X = halogen) and I (R = H). E.g., 7.6 g I (R = R1 = R2 = H). HBr in 80 ml DMF contg. 10 g Na2CO3 was heated at 80-95.degree. with 4.2 g Me2N(CH2)3Cl, the ppt. obtained dissolved in CHCl3 and washed with satd. aq. NaCl soln. to give 4 g I (R = Me2N(CH2)3, R1 = R2 = H).cntdot.2HCl.
IT 54950-45-78
RI: SPN (Synthetic preparation); PREP (Preparation)
GI (prepn. of)
RN 54950-45-7 CAPLUS
CN 1-Thia-4,8-diazaspiro[4.5]decan-3-one, 8-[2-(4-phenyl-1-piperazinyl)ethyl]-

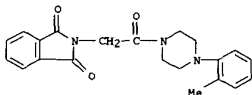
L14 ANSWER 253 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1974:505444 CAPLUS
DOCUMENT NUMBER: 81:105444
TITLE: Possible antiparkinsonian compounds. I. Synthesis of N-aryl/alkyl-N'-phthaloyl glycolyl-dl-alpha. (-alanine)piperazines
AUTHOR(S): Tiwari, S. S.; Pandey, V. K.
CORPORATE SOURCE: Dep. Chem., Lucknow Univ., Lucknow, India
SOURCE: Indian J. Appl. Chem. (1972), 35(4-6), 85-6
CODEN: IJACAN
DOCUMENT TYPE: Journal
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB The piperazines I (R = Ph, p-MeC6H4, Me, p-ClC6H4, etc.; R1 = H, Me) were prepd. by treating phthaloylacyl chlorides with piperazines.
IT 53646-59-6P 53646-60-9P 53646-61-0P 53646-62-1P 53646-63-2P 53646-64-3P 53646-65-4P 53646-66-5P
RI: SPN (Synthetic preparation); PREP (Preparation)
GI (prepn. of)
RN 53646-59-6 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(4-methylphenyl)- (9CI) (CA INDEX NAME)



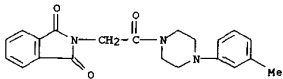
RN 53646-60-9 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-phenyl- (9CI) (CA INDEX NAME)



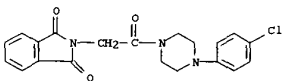
RN 53646-61-0 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



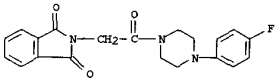
RN 53646-62-1 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(3-methylphenyl)- (9CI) (CA INDEX NAME)



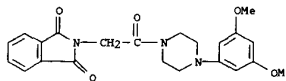
RN 53646-63-2 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(4-chlorophenyl)- (9CI) (CA INDEX NAME)



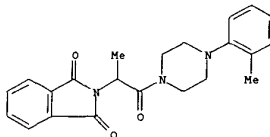
RN 53646-64-3 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(4-fluorophenyl)- (9CI) (CA INDEX NAME)



RN 53646-65-4 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(3,5-dimethoxyphenyl)- (9CI) (CA INDEX NAME)



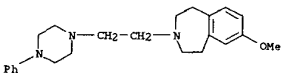
RN 53646-66-5 CAPLUS
CN Piperazine, 1-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)acetyl]-4-(2-methylphenyl)- (9CI) (CA INDEX NAME)



L14 ANSWER 254 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1974:82731 CAPLUS
DOCUMENT NUMBER: 80:82731
TITLE: 1,2,4,5-Tetrahydro-3H,3-benzazepines
INVENTOR(S): Shetty, Bola V.
PATENT ASSIGNEE(S): Pennwalt Corp.
SOURCE: Fr. Demande, 73 pp.
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| FR 2171879 | A1 | 19730928 | FR 1972-4829 | 19720214 |
| FR 2171879 | B1 | 19750425 | | |

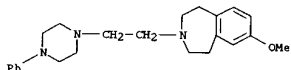
GI For diagram(s), see printed CA issue.
AB Benzazepines I (R = CH₂CH₂OMe₂, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, allyl, 2-(4-phenylpiperazino)-ethyl, CH₂OMe:CH₂, CH₂C.tplbond.CH, Me, Et, Pr, CH₂CH₂Ph, CHMeCH₂Ph, CH₂CH₂C₆H₄NH₂-p, CH₂CH₂C₆H₄NHAc-p, CH₂CH:CHPh, trans-2-phenylcyclopropylmethyl, CH₂CH₂OAc, CH₂CH₂OMeOAc, CHMeCH₂C₆H₄NH₂-p) were prepd. by substitution of I (R = H).
I (R = H, R₁ = Me) was prepd. by methylating 3,4-Me₂C₆H₃OH, oxidizing the 3,4-Me₂C₆H₃OMe, converting the 4-MeOC₆H₄(CO₂H) 2-1,2 to its anhydride, reducing to 4-MeOC₆H₄(CH₂OH) 2-1,2, and converting to 4-MeOC₆H₄(CH₂Br) 2-1,2 and 4-MeOC₆H₄(CH₂CN) 2-1,2, which was cyclized to 7-methoxy-1,2,4,5-tetrahydro-3H-3-benzazepine-2,4-dione and reduced with BH₃.
Demethylation with HBr gave I (R = R₁ = H). I are analgesics and narcotic antagonists.
Thus, I (R = CH₂CH₂C₆H₄NHAc-p, R₁ = Me) had an oral ED₅₀ in the writhing test of 32 mg/kg.
IT 36134-36-8P
RL: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
RN 36134-36-8 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)



L14 ANSWER 255 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1973:526338 CAPLUS
DOCUMENT NUMBER: 79:126338
TITLE: 1,2,4,5-tetrahydro-3H-3-benzazepines
INVENTOR(S): Shetty, Bola V.
PATENT ASSIGNEE(S): Pennwalt Corp.
SOURCE: Ger. Offen., 82 pp.
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| DE 2207430 | A1 | 19730823 | DE 1972-2207430 | 19720214 |
| DE 2207430 | B2 | 19810723 | | |
| DE 2207430 | C3 | 19820513 | | |

GI For diagram(s), see printed CA Issue.
AB Benzazepines I (R = H, CH₂CH₂OMe, CH₂CH₂CHPh, allyl, CH₂C.tpbond, CH, cyclopropylmethyl, cyclobutylmethyl, cyclopentylmethyl, trans-2-phenylcyclopropylmethyl, Me, Et, Pr, CH₂CH₂Ph, CHMeCH₂Ph, CH₂CH₂C₆H₄NH₂-p, CHMeCH₂C₆H₄NH₂-p, CH₂CH₂C₆H₄NHAc-p, CH₂CH₂OAc, (CH₂)₃OMe, 4-phenylpiperazinylethyl; R1 = H, Me) were prepd. Thus, 3,4-Me₂C₆H₃OH was methylated and oxidized to give 3,4-(HO₂C)C₆H₃OMe, whose anhydride was reduced to 3,4-(HOCH₂)C₆H₃OMe, brominated to 3,4-(BrCH₂)C₆H₃OMe, treated with NaCN to give 3,4-(NCCH₂)C₆H₃OMe, which was cyclized with HBr-HOAc to 7-methoxy-1,2,4,5-tetrahydro-3H-3-benzazepine-2,4-dione and reduced with B₂H₆ to I (R = H, R1 = Me) from which the other I were derived. I demonstrated antihistaminic, analgesic, anticholinergic, and morphine antagonist activity.
IT 36134-35-7P 36134-36-8P
RL: SPN (Synthetic preparation); PREP (Preparation)
RN 36134-35-7 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

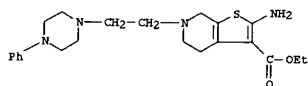


RN 36134-36-8 CAPLUS
CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

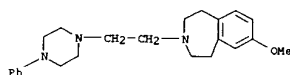
L14 ANSWER 256 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1973:466340 CAPLUS
DOCUMENT NUMBER: 79:66340
TITLE: Aminoalkylthienopyridine derivatives
INVENTOR(S): Nakanishi, Michio; Tahara, Tetsuji
PATENT ASSIGNEE(S): Yoshitomi Pharmaceutical Industries, Ltd.
SOURCE: Jpn. Tokkyo Koho, 5 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| JP 48015957 | B4 | 19730518 | JP 1969-104694 | 19691224 |

GI For diagram(s), see printed CA Issue.
AB The title deriva. I, Useful as antiinflammatory and antidiuretic remedies, were prepd. E.g., a mixt. of 1-(2-dimethylaminoethyl)-4-piperidone, CNCH₂CO₂Et, and S in EtOH was kept 1.5 hr at 60-70.degree., cooled, and (CO₂H) 2 in EtOH added to give 63.2% I dioxalate (R = Me, R1 = EtCO₂, n = 2). Similarly, the following I were prepd. (R, R1, n given): piperidino, EtCO₂, 3; pyrrolidino, EtCO₂, 3; Et, EtCO₂, 2; morpholino, NH₂CO, 2; Me, EtCO₂, 3; Et, CN, 2; morpholino, EtCO₂, 2; 4-phenyl-1-piperazinyl, EtCO₂, 2; piperidino, Bz, 3; and pyrrolidino, BuCO₂, 3.
IT 42026-24-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
RN 42026-24-4 CAPLUS
CN Thieno[2,3-c]pyridine-3-carboxylic acid, 2-amino-4,5,6,7-tetrahydro-6-[2-(4-phenyl-1-piperazinyl)ethyl]-, ethyl ester (9CI) (CA INDEX NAME)



L14 ANSWER 255 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



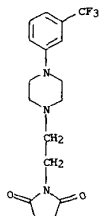
● 2 HCl

L14 ANSWER 257 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1973:159666 CAPLUS
DOCUMENT NUMBER: 78:159666
TITLE: Anorexicogenic 1-ethyl-4-[m-(trifluoromethyl)phenyl]piperazine derivatives
INVENTOR(S): Cross, Peter E.
PATENT ASSIGNEE(S): Pfizer Corp.
SOURCE: Ger. Offen., 27 pp.
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| DE 2242382 | A1 | 19730315 | DE 1972-2242382 | 19720829 |
| AU 7245940 | A1 | 19740228 | AU 1972-45940 | 19720824 |
| NL 7211694 | A | 19730306 | NL 1972-11694 | 19720828 |
| BE 788280 | A1 | 19730228 | BE 1972-121582 | 19720831 |
| FR 2154449 | A1 | 19730511 | FR 1972-31080 | 19720901 |
| CH 551430 | A | 19740715 | CH 1974-3568 | 19720901 |
| CH 554899 | A | 19741015 | CH 1972-12935 | 19720901 |
| AT 320655 | B | 19750225 | AT 1973-10895 | 19720901 |
| AT 321307 | B | 19750325 | AT 1972-7520 | 19720901 |
| JP 48085584 | A2 | 19731113 | JP 1972-88020 | 19720904 |
| ES 406374 | A1 | 19750716 | ES 1972-406374 | 19720904 |

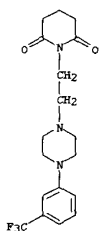
PRIORITY APPLN. INFO.: GB 1971-41322 19710904
GB 1972-20536 19720503

GI For diagram(s), see printed CA Issue.
AB Eight title compds. (I, R = H, Cl, or Br; R1 = e.g. succinimido, glutarimido, or 2,4-dioxo-3-imidazolidinyl) and (or) their HCl salts were prepd. and used as appetite depressants. Thus, 11.5 g 1-[m-(trifluoromethyl)-phenyl]piperazine, 8.1 g .beta.-succinimidoethyl chloride, K₂CO₃, and MeI were heated in DMF for 24 hr at 100.degree. to give 9.1 g I.HCl (R = H, R1 = succinimido).
IT 41212-97-9P 41212-99-1P 41213-05-2P 41213-07-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
RN 41212-97-9 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-[3-(trifluoromethyl)phenyl]-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



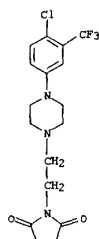
● HCl

RN 41212-99-1 CAPLUS
CN 2,6-Piperidinedione, 1-[2-[4-(3-(trifluoromethyl)phenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



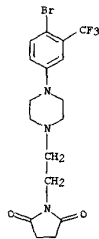
● HCl

RN 41213-05-2 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(4-chloro-3-(trifluoromethyl)phenyl)-1-piperazinyl]ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)

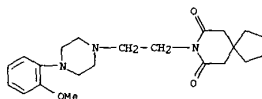


● HCl

RN 41213-07-4 CAPLUS
CN 2,5-Pyrrolidinedione, 1-[2-[4-(4-bromo-3-(trifluoromethyl)phenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



L14 ANSWER 258 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1972:443062 CAPLUS
DOCUMENT NUMBER: 77:43062
TITLE: Psychoedative agents. 2. 8-(4-Substituted 1-piperazinylalkyl)-8-azaspiro[4.5]decane-7,9-diones
AUTHOR(S): Wu, Yao-Rua; Rayburn, J. W.; Allen, L. E.; Ferguson,
CORPORATE SOURCE: H. C.; Kissel, J. W.
Evansville, Dep. Chem. Res., Mead Johnson Res. Cent.,
INDIANA, USA
SOURCE: J. Med. Chem. (1972), 15(5), 477-9
CODEN: JMCHEM
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Several of the title compds. synthesized had greater potency and selectivity as tranquilizers than chlorpromazine [50-53-3]. Thus, 2-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-dione (I) [33386-08-2] had an ED50 for complete suppression of conditioned avoidance response of 4.3 mg/kg i.p. in rats; 19.6 times this dose was required for complete suppression of the unconditioned escape response. Corresponding data for the 2-pyridyl analog and chlorpromazine were 2.8 and 4.8 mg/kg, and 12.1 and 10.2 times, resp. I produced much less sedation than chlorpromazine, had very little .alpha.-adrenergic blocking activity in vivo and in vitro, and had an LD50 of 146 mg/kg i.p. in mice. The incidence of catalepsy induced by I in monkeys was similar to that with chlorpromazine. To synthesize I, N-(2-pyrimidinyl)piperazine was prepd. from piperazine and 2-chloropyrimidine by nucleophilic aromatic substitution, reacted with .omega.-chloropropionitrile, reduced with LiAlH4 or Raney Ni-H2 to 1-(.omega.-aminobutyl)-4-(2-pyrimidinyl)piperazine, and reacted with the spiro compd. cyclopentane-1,1-diacetic acid anhydride.
IT 21102-95-4
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(tranquilizing activity of)
RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

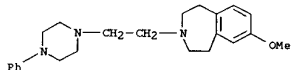


● 2 HCl

L14 ANSWER 259 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1972:153628 CAPLUS
 DOCUMENT NUMBER: 76:153628
 TITLE: 1,2,4,5-Tetrahydro-3H-3-benzazepines as
 analgesics and antagonists of narcotics
 PATENT ASSIGNEE(S): Wallace and Tiernan, Inc.
 SOURCE: Brit., 42 pp.
 CODEN: BRXXAA
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|------|
| GB 1268243 | | 19720322 | | |

PRIORITY APPLM. INFO.: US 1968-711897 19680311
 GI For diagram(s), see printed CA Issue.
 AB H-3-Benzazepines (I, R was usually 7- or 8-MeO or 7-OH; R1 was, e.g., H, alkyl, cycloalkylmethyl, substituted phenethyl, p-MeC6H4SO2, a ceoxyalkyl; R2 = H3 Me), useful as analgesics, anticholinergics, antihistamines, and antagonists to narcotics, were prepd. Thus, 50 g 4-methoxy-.omicron.-benzenediacetamide (II) was reduced by borane in THF at 10.degree. to give 28 g I (R = 7-MeO, R1 = R2 = H), analyzed as the maleate. II was prepd. from 3,4-dimethylphenol by methylation, oxidn. to 4-methoxyphthalic acid, formation of the an-hydrate, redn. to 4-methoxy-.omicron.-xylene-.alpha.,.alpha.'-diol, dibromination of the diol, conversion to the dinitrile, and cyclization to the imide. Pharmacol. test results were given.
 IT 36134-35-7P 36134-36-8P
 RI: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
 RN 36134-35-7 CAPLUS
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

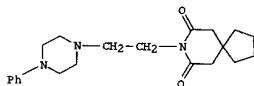


RN 36134-36-8 CAPLUS
 CN 1H-3-Benzazepine, 2,3,4,5-tetrahydro-7-methoxy-3-[2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 260 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1971:125435 CAPLUS
 DOCUMENT NUMBER: 74:125435
 TITLE: Pharmacologic compositions containing azaspirodecanediones and azaspirodecanediones
 INVENTOR(S): Wu, Yao Hua
 PATENT ASSIGNEE(S): Mead Johnson and Co.
 SOURCE: U.S., 6 pp. Continuation-in-part of U.S. 3,398,151
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| US 3558777 | A | 19710126 | US 1968-738848 | 19680621 |

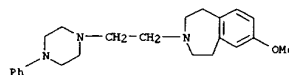
AB The disclosure is similar, but the claims are different.
 IT 21090-08-4P 21102-95-4P 21102-99-8P
 RI: SPN (Synthetic preparation); PREP (Preparation) (prepn. of)
 RN 21090-08-4 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

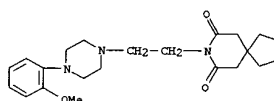
RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 259 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



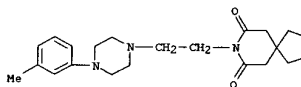
● 2 HCl

L14 ANSWER 260 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



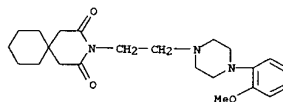
● 2 HCl

RN 21102-99-8 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

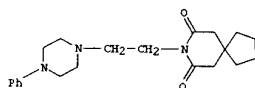
RN 25024-82-2 CAPLUS
 CN 1,1-Cyclohexanediacetamide, N-[2-[4-(o-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

RS1.551.

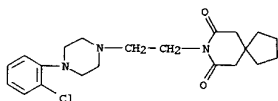
L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1969:500204 CAPLUS
 DOCUMENT NUMBER: 71:100204
 TITLE: Psychosedative agents. N-(4-phenyl-1-piperazinyllalkyl)-substituted cyclic imides
 Wu, Yao-Hua; Smith, Kenneth R.; Rayburn, James W.
 AUTHOR(S): Kissel, John W.
 CORPORATE SOURCE: Dep. Pharmacol., Mead Johnson Res. Center, Evansville, Indiana, USA
 SOURCE: J. Med. Chem. (1969), 12, 876-81
 CODEN: JMCMAR
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Fifty-two N-substituted cyclic imides bearing a 4-phenyl-1-piperazinyllalkyl moiety were synthesized and screened as psychosedative agents. The results of 2 test methods, (a) antagonism of amphetamine-aggregation stress in mice and (b) suppression of the conditioned avoidance response in rats, indicate that these compds. possess in varying degrees psychotropic properties typical of major tranquilizers.
 IT 21090-08-4 21102-95-4 21102-99-8
 21103-15-1 21103-17-3 21103-21-9
 21103-24-2 25024-54-8 25024-66-2
 25024-74-2 25024-76-4 25024-82-2
 25024-84-4 25024-90-2 25024-91-3
 25024-92-4 25024-93-5 25024-94-6
 RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
 (tranquilizing activity of)
 RN 21090-08-4 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

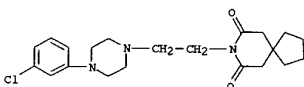
RN 21102-95-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(2-methoxyphenyl)-1-piperazinyl)ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



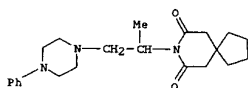
● HCl

RN 21103-21-9 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[2-[4-(m-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

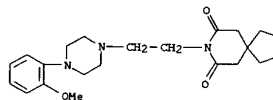
RN 21103-24-2 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[1-methyl-2-(4-phenyl-1-piperazinyl)ethyl]-, dihydrochloride (8CI) (CA INDEX NAME)



● 2 HCl

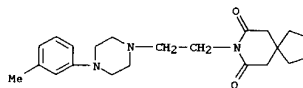
RN 25024-54-8 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[2-(4-o-tolyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



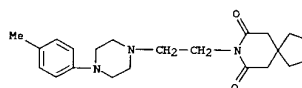
● 2 HCl

RN 21102-99-8 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

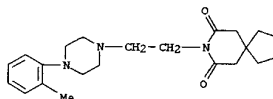
RN 21103-15-1 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[2-(4-p-tolyl-1-piperazinyl)ethyl]-, dihydrochloride (8CI) (CA INDEX NAME)



● 2 HCl

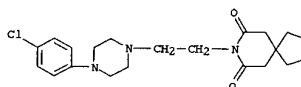
RN 21103-17-3 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[2-[4-(o-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

L14 ANSWER 261 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)



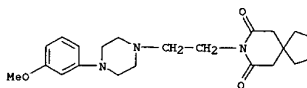
● HCl

RN 25024-66-2 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[2-[4-(p-chlorophenyl)-1-piperazinyl]ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



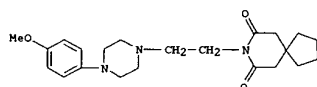
● HCl

RN 25024-74-2 CAPLUS
 CN 1,1-Cyclopentanediacetamide, N-[2-[4-(m-methoxyphenyl)-1-piperazinyl]ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)



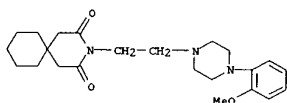
● HCl

RN 25024-76-4 CAPLUS
 CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-(4-methoxyphenyl)-1-piperazinyl)ethyl]-, monohydrochloride (9CI) (CA INDEX NAME)



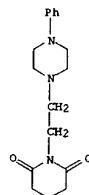
● HCl

RN 25024-82-2 CAPLUS
CN 1,1-Cyclohexanediacetamide,
N-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-,
monohydrochloride (8CI) (CA INDEX NAME)



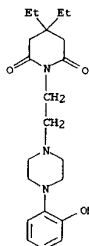
● HCl

RN 25024-84-4 CAPLUS
CN Glutarimide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride
(8CI)
(CA INDEX NAME)



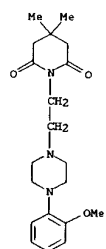
● HCl

RN 25024-90-2 CAPLUS
CN Glutarimide,
3,3-diethyl-N-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-,
monohydrochloride (8CI) (CA INDEX NAME)



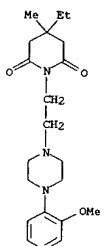
● HCl

RN 25024-91-3 CAPLUS
CN Glutarimide,
N-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-3,3-dimethyl-,
dihydrochloride (8CI) (CA INDEX NAME)



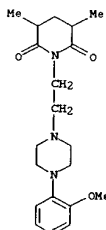
● 2 HCl

RN 25024-92-4 CAPLUS
CN Glutarimide,
3-ethyl-N-[2-[4-(4-methoxyphenyl)-1-piperazinyl]ethyl]-3-
methyl-, dihydrochloride (8CI) (CA INDEX NAME)

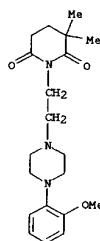


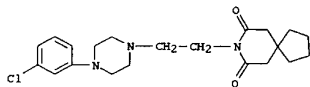
● 2 HCl

RN 25024-93-5 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,5-
dimethyl- (9CI) (CA INDEX NAME)



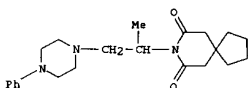
RN 25024-94-6 CAPLUS
CN 2,6-Piperidinedione,
1-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-3,3-
dimethyl- (9CI) (CA INDEX NAME)



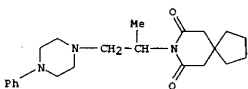


● HCl

RN 21103-23-1 CAPLUS
 CN 1,1-Cyclopentanediacetamide,
 N-[1-methyl-2-(4-phenyl-1-piperazinyl)ethyl]-
 (8Cl) (CA INDEX NAME)



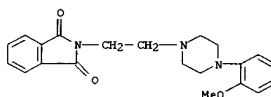
RN 21103-24-2 CAPLUS
 CN 1,1-Cyclopentanediacetamide,
 N-[1-methyl-2-(4-phenyl-1-piperazinyl)ethyl]-
 , dihydrochloride (8Cl) (CA INDEX NAME)



● 2 HCl

L14 ANSWER 263 OF 263 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1968:410474 CAPLUS
 DOCUMENT NUMBER: 69:10474
 TITLE: Preparation of phthalimidoalkyl piperazines
 INVENTOR(S): Lavrinovics, E.; Grinsteins, V.
 SOURCE: U.S.S.R.
 CODEN: URXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Russian
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|---|-----------|-----------------|-----------|
| SU 193524 | | 1967/0313 | SU | 1966/0407 |
| AB | From Izobret., Prom. Obratzy, Tovarye Znaki 1967, 44(7), 39. N-Arylpiperazine is treated with N-haloalkylphthalimide in MeOH under reflux to yield the title compds. | | | |
| IT | 18503-07-6P RL: SPN (Synthetic preparation); PREF (Preparation) (prepn. of) | | | |
| RN | 18503-07-6 CAPLUS | | | |
| CN | Phthalimide, N-[(4-(o-methoxyphenyl)-1-piperazinyl)methyl]-, monohydrobromide (8Cl) (CA INDEX NAME) | | | |



● HBr

L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1969:4143 CAPLUS
DOCUMENT NUMBER: 70:4143
TITLE: Azaspirodecanediones and azaspirodecanediones
INVENTOR(S): Wu, Yao Hua
PATENT ASSIGNEE(S): Head Johnson and Co.
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

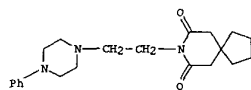
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|----------|-----------------|----------|
| US 3398151 | A | 19680820 | US 1967-607908 | 19670109 |

GI For diagram(s), see printed CA issue.
AB 8-(4-Phenyl-1-piperazinylalkylene)-8-azaspiro[4.5]decane-7,9-diones [I, n = 2, A = (CH₂)_n] having 0-3 substituents in the Ph ring were synthesized from the corresponding 4-phenylpiperazines and 3,3-tetramethyleneglutaric anhydride (II). Employing 3,3-pentamethyleneglutaric anhydride in the method yielded the 3-azaspiro[5.5]undecane-2,4-dione analog. These substances have strong activity and good selectivity in suppressing conditioned avoidance response in animals and are useful as psychotropic agents, analgetics, centrally acting muscle relaxants, capillary protectants, antiallergic agents, anti-inflammatory agents, and antiemetics. Thus, a mixt. of 0.1 mole of the substituted glutaric anhydride, 0.1 mole 1-(4- ω -aminoalkyl)-4-phenylpiperazine, and 400 ml. CSH₅N was refluxed 15 hrs., the solvent distd., and the residue purified by distn. in vacuo or crystn. If the residue contained amide and carbonyl bands in the ir, it was refluxed with 10 parts by wt. Ac₂O for 15 hrs. prior to purification as above. The HCl salt of the free base was prepd. by treating the EtOH soln. of the free base with an equiv. amt. of ethanolic HCl soln. The following I were thus obtained (n A, R, b.p./mm. % yield, m.p. of HCl salt, and crystn. solvent given): 4, (CH₂)₂, H 215-35.degree./0.45, 80, 135-7.degree. (decompn.), iso-PrOH; 4, (CH₂)₃, H 250-2.degree./0.5, 80, 234.5-6.5.degree. (decompn.), iso-PrOH-EtOH; 4, (CH₂)₄, H, 260-75.degree./0.1, 82.8, 218.5-20.5.degree. (decompn.), iso-PrOH; 4, (CH₂)₅, H, 253-63.degree./0.2, 89, 188.5-96.5, EtOH; 5, (CH₂)₃, H, 263-76.degree./0.15-0.25, 77.8, 254-5.degree. (decompn.), EtOH; 5, (CH₂)₂, o-Me, 230-60.degree./0.2, 92, 211-12.degree. (decompn.), EtOH; 4, (CH₂)₂, o-Me (III), 220-40.degree./0.35, 77, 196.5-8.5.degree.

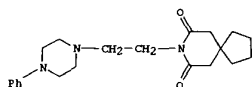
L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
phenylpiperazine, b0.15 155-68.degree., m. 81-3.degree., prepd. in 65% yield from 3-chloro-2-methylbutyronitrile by the above procedure, was dissolved (0.04 mole) in 100 ml. tetrahydrofuran, the soln. added dropwise with vigorous stirring during 35 min. to a suspension of 1.87 g. LiAlH₄ in 100 ml. Et₂O and refluxed, and the residue distd. in vacuo to give 81.7% 1-(4-amino-2-methylbutyl)-4-phenylpiperazine, b0.17 138-55.degree., n_D20 1.5485. A stirred mixt. of 16.8 g. II and 200 ml. CSH₅N was treated with 12.2 g. ethanalamine, refluxed 3 hrs., and fractionally distd. in vacuo to give 12.0 g. 8-(2-hydroxyethyl)-8-azaspiro[4.5]decane-7,9-dione [(VII), A = (CH₂)₂, X = OH] (VIIa), b0.05-0.1 142-50.degree., n_D20 1.5150. A cooled mixt. (10-15.degree.) of 6.0 g. VIIa, 50 ml. C₆H₆, and 2.4 g. CSH₅N was treated dropwise during 25 min. with 3.6 g. SOCl₂, heated 1 hr. at 60-5.degree., and filtered, the filtrate treated with 20 ml. distd. H₂O, and the C₆H₆ layer sepd., dried, and fractionally distd. in vacuo to give 4.5 g. 8-(2-chloroethyl)-8-azaspiro[4.5]decane-7,9-dione [(VII), A = (CH₂)₂, X = Cl] (VIIb), b0.05 120-2.degree., n_D20 1.5139. The following VII were similarly prepd. (A, X, b.p./mm., and % yield given): (CH₂)₃, OH, 155-70.degree./0.1-0.15, 62; (CH₂)₃, Cl, 155-62.degree./0.06, 73; (CH₂)₂(CH₂)₂, OH, 191-204.degree./0.08-0.18, 80.7; (CH₂)₂(CH₂)₂, Cl, 155-65.degree./0.25, 50; (CH₂)₄, OH, 185-240.degree./0.2, 74.9; (CH₂)₄, Cl, 160-95.degree./0.3, 53.5. A mixt. of 23 g. VIIb, 19.2 g. IV, and 31.8 g. anhyd. Na₂CO₃ in 400 ml. C₆H₆ was refluxed 15 hrs., and filtered, and the filtrate fractionally distd. to give III. The following I were similarly prepd. (n, A, R, b.p./mm., % yield, and m.p. of HCl salt given): 4, (CH₂)₃, p-MeO, 220-45.degree./0.1, 65, 225.5-6.5.degree. (decompn.); 4, (CH₂)₂(CH₂)₂, o-MeO, 240-60.degree./0.2, 20, 206.5-8.5.degree.; 4, (CH₂)₂(CH₂)₂, H, 190-260.degree./0.25-0.35, 86, 155-7.degree.; 4, (CH₂)₃, m-Me, 160-85.degree./0.5-0.1, 92, 240.5-2.5.degree. (decompn.); 4, (CH₂)₃, H, 240-60.degree./0.2, 69, 217.5-18.5.degree.; 4, (CH₂)₄, o-F, -, -, 188-90.degree.; 4, (CH₂)₄, o-MeSO₂NH, -, 73.5, 263.5-4.5.degree.; 4, (CH₂)₄, o-NO₂, 150-80.degree./0.1, 26.8, -. I contg. multiple substituents in the Ph ring were similarly prepd. and were tabulated but not characterized. A mixt. of 15.28 g. II, 200 ml. CSH₅N, and 5.0 g.

L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
(decompn.), EtOH; 4, (CH₂)₃, o-Me, 220-50.degree./0.11, 90, 208.5-10.5.degree. (decompn.), iso-PrOH; 4, (CH₂)₂, m-Me, 225-35.degree./0.3, 81, 205.5-7.0.degree. (decompn.), iso-PrOH; 4, (CH₂)₃, o-Cl, 215-45.degree./0.1, 94, 234.5-5.5.degree. (decompn.), iso-PrOH; 4, (CH₂)₃, m-Me, 200-60.degree./0.1, 70, 235.5-7.0.degree. (decompn.), EtOH; 4, (CH₂)₂CM₂CH₂, H, 235-50.degree./0.25, 80, 207.5-12.0.degree., iso-PrOH; 4, (CH₂)₄, o-Me, 243-7.degree./0.18, 89.6, 199.5-203.degree., EtOH; 4, (CH₂)₄, o-Cl, 240-60.degree./0.2, 90, 238.5-41.0.degree., EtOH; 4, (CH₂)₄, o-Me, 230-70.degree./0.1, 95, 202-3.5.degree., EtOH; 4, (CH₂)₄, o-Me, 255.degree./0.01, 86, 246-7.5.degree., EtOH; 4, (CH₂)₃, o-Me, 230-50.degree./0.3, 90, 254.5-5.5.degree. (decompn.), iso-PrOH; 4, (CH₂)₅, o-Me, -, 88, 174.5-6.5.degree., EtOH-Et₂O; 4, (CH₂)₃, p-Me, 160-80.degree./0.1, 75, 247-8.degree. (decompn.), iso-PrOH; 4, (CH₂)₂, p-Me, 165-200.degree./0.05-0.1, 73, 236.5-8.5.degree. (decompn.), iso-PrOH; 4, (CH₂)₂, o-Cl, 165-84.degree./0.1, 80, 241-2.5.degree. (decompn.), iso-PrOH; 4, (CH₂)₃, m-Cl, 164-70.degree./0.1, 68, 248.5-50.5.degree. (decompn.), iso-PrOH; 4, (CH₂)₂, m-Cl, 140-210.degree./0.5-0.1, 74, 226.5-8.5.degree. (decompn.), iso-PrOH; 4, (CH₂)₃, p-Cl, 175-97.degree./0.1, 90, 248-9.degree. (decompn.), EtOH; 4, CM₂CH₂, H, 230-40.degree./0.25, 87, 255.5-7.5.degree., EtOH. A stirred mixt. of 19.2 g. 1-(o-methoxyphenyl)-piperazine (IV), 9.0 g. ClCH₂CH₂CN, 150 ml. C₆H₆, and 16.6 g. anhyd. Na₂CO₃ was refluxed overnight under anhyd. conditions and filtered, the filter cake washed with C₆H₆, and the combined C₆H₆ filtrates fractionally distd. in vacuo to give 19.6 g. 1-(2-cyanoethyl)-4-(o-methoxyphenyl)piperazine (V), b1 208-26.degree., m. 72-4.degree.. A mixt. of 8.1 g. V, 30 g. dry liq. NH₃, and 100 ml. abs. MeOH was hydrogenated at 1200 psi. and room temp. over W-6 Raney Ni to give 85% 1-(3-aminopropyl)-4-(o-methoxyphenyl)piperazine (VI, A = (CH₂)₃, R = o-MeO). The following VI were similarly prepd. (except that the last five compds. were prepd. by redn. with LiAlH₄, an example of which is given below) (A, R, % yield, b.p./mm., and n_D20 given): (CH₂)₂, m-Me, 85.5, 117-34.degree./0.3, 1.5638; (CH₂)₃, m-Me, 68.8, 115-65.degree./0.15, 1.5561; (CH₂)₃, m-Me, 48.0, 120.degree./0.18, 1.5656; (CH₂)₃, m-Cl, 79, 142-70.degree./0.15-0.5, -, (CH₂)₃, m-Cl, 62, 108-40.degree./0.1-0.15, 1.5827; (CH₂)₂CM₂CH₂, H, 81.7, 138-55.degree./0.17, 1.5485; (CH₂)₄, o-MeO, 79.6, 150-60.degree./0.25, 1.5496; (CH₂)₄, o-Cl, 74.0, 130-65.degree./0.15-0.35, 1.5560; (CH₂)₄, o-Me, 32.8, 145-60.degree./0.08, -, (CH₂)₅, o-MeO, 57.6, 163-72.degree./0.2, 1.5444. 1-(3-Cyano-2-methylpropyl)-4-

L14 ANSWER 262 OF 263 CAPLUS COPYRIGHT 2002 ACS (Continued)
propargylamine was refluxed overnight in the absence of moisture and fractionally distd. in vacuo (b0.15 129-45.degree.) to give crude 8-propargyl-8-azaspiro[4.5]decane-7,9-dione (VIII) contaminated with II. A mixt. of 6.0 g. VIII, 2.4 g. 37% aq. HCHO, a few crystals of CuCl (catalyst), 1.78 g. AcOH, 2.9 g. distd. H₂O, and 4.8 g. 1-phenylpiperazine was heated under N on a water bath at 40.degree. 7 hrs., extd. with 3 times. 75 ml. CHCl₃, and worked up in the usual manner, and the product converted to the HCl salt to give 6.5 g. 8-[4-(4-phenyl-1-piperazinyl)-2-butyryl]-8-azaspiro[4.5]decane-7,9-dione dihydrochloride, m. 173-4.degree. (EtOH). Similarly prepd. was 8-[4-(4-o-methoxyphenyl-1-piperazinyl)-2-butyryl]-8-azaspiro[4.5]decane-7,9-dione dihydrochloride, m. 172-5.degree..
IT 21090-07-3P 21090-08-4P 21102-92-1P
21102-93-2P 21102-94-3P 21102-95-4P
21102-96-5P 21102-98-6P 21103-34-0P
21103-15-1P 21103-16-2P 21103-17-3P
21103-20-6P 21103-21-9P 21103-23-1P
21103-24-2P
RL: SPN (Synthetic preparation); PREP (Preparation) (prep. of)
RN 21090-07-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-(4-phenyl-1-piperazinyl)ethyl]- (9CI) (CA INDEX NAME)

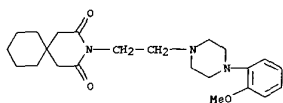


RN 21090-08-4 CAPLUS
CN 1,1-Cyclopentenediacetamide, N-[2-(4-phenyl-1-piperazinyl)ethyl]-, monohydrochloride (8CI) (CA INDEX NAME)

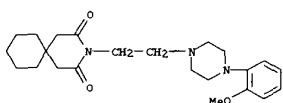


● HCl

RN 21102-92-1 CAPLUS
CN 1,1-Cyclohexanediacectimide,
N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-
(8CI) (CA INDEX NAME)

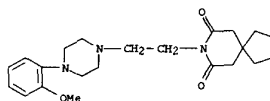


RN 21102-93-2 CAPLUS
CN 1,1-Cyclopentanediacetamide,
N-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-
, hydrochloride (8CI) (CA INDEX NAME)

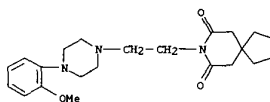


● x HCl

RN 21102-94-3 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)

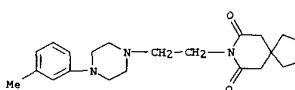


RN 21102-95-4 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(2-methoxyphenyl)-1-piperazinyl]ethyl]-, dihydrochloride (9CI) (CA INDEX NAME)

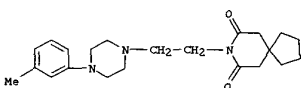


● 2 HCl

RN 21102-98-7 CAPLUS
CN 1,1-Cyclopentanediacetamide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-
(8CI) (CA INDEX NAME)

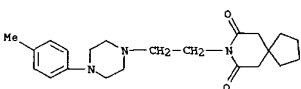


RN 21102-99-8 CAPLUS
CN 1,1-Cyclopentanediacetamide, N-[2-(4-m-tolyl-1-piperazinyl)ethyl]-,
monohydrochloride (8CI) (CA INDEX NAME)

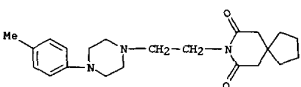


● HCl

RN 21103-14-0 CAPLUS
CN 1,1-Cyclopentanediacetamide, N-[2-(4-p-tolyl-1-piperazinyl)ethyl]-
(8CI) (CA INDEX NAME)

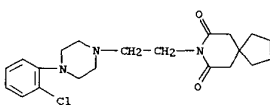


RN 21103-15-1 CAPLUS
CN 1,1-Cyclopentanediacetamide, N-[2-(4-p-tolyl-1-piperazinyl)ethyl]-,
dihydrochloride (8CI) (CA INDEX NAME)

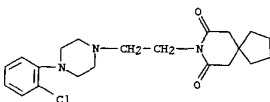


● 2 HCl

RN 21103-16-2 CAPLUS
CN 1,1-Cyclopentanediacetamide,
N-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-
(8CI) (CA INDEX NAME)

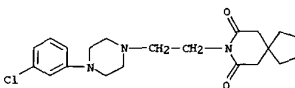


RN 21103-17-3 CAPLUS
CN 1,1-Cyclopentanediacetamide,
N-[2-[4-(2-chlorophenyl)-1-piperazinyl]ethyl]-
, monohydrochloride (8CI) (CA INDEX NAME)



● HCl

RN 21103-20-8 CAPLUS
CN 8-Azaspiro[4.5]decane-7,9-dione, 8-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]- (9CI) (CA INDEX NAME)



RN 21103-21-9 CAPLUS
CN 1,1-Cyclopentanediacetamide,
N-[2-[4-(3-chlorophenyl)-1-piperazinyl]ethyl]-
, monohydrochloride (8CI) (CA INDEX NAME)

L6 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1972:443062 CAPLUS

DOCUMENT NUMBER: 77:43062

TITLE: **Psychosedative** agents. 2. 8-(4-Substituted
1-piperazinylalkyl)-8-azaspiro[4.5]decane-7,9-diones
AUTHOR(S): Wu, Yao-Hua; Rayburn, J. W.; Allen, L. E.; Ferguson,
H. C.; Kissel, J. W.

CORPORATE SOURCE: Dep. Chem. Res., Mead Johnson Res. Cent., Evansville,
Indiana, USA

SOURCE: J. Med. Chem. (1972), 15(5), 477-9

CODEN: JMCMAR

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Several of the title compds. synthesized had greater potency and
selectivity as tranquilizers than chlorpromazine [50-53-3]. Thus,
2-[4-[4-(2-pyrimidinyl)-1-piperazinyl]butyl]-8-azaspiro[4.5]decane-7,9-
dione (I) [33386-08-2] had an ED50 for complete suppression of

conditioned

avoidance response of 4.3 mg/kg i.p. in rats; 19.6 times this dose was
required for complete suppression of the unconditioned escape response.
Corresponding data for the 2-pyridyl analog and chlorpromazine were 2.8
and 4.8 mg/kg, and 12.1 and 10.2 times, resp. I produced much less
sedation than chlorpromazine, had very little .alpha.-**adrenergic**
blocking activity in vivo and in vitro, and had an LD50 of 146 mg/kg i.p.
in mice. The incidence of catalepsy induced by I in monkeys was similar
to that with chlorpromazine. To synthesize I,

N-(2-pyrimidinyl)piperazine

was prepd. from piperazine and 2-chloropyrimidine by nucleophilic
aromatic

substitution, reacted with .omega.-chloropropionitrile, reduced with
LiAlH₄ or Raney Ni-H₂ to 1-(.omega.-aminobutyl)-4-(2-
pyrimidinyl)piperazine, and reacted with the spiro compd.
cyclopentane-1,1-diacetic acid anhydride.

L9 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:260493 CAPLUS

DOCUMENT NUMBER: 126:312328

TITLE: Recent advances in the identification of .
alpha.1- and **alpha.2** adrenoceptor
subtypes: therapeutic implications

AUTHOR(S): Hieble, J. Paul; Rufolo, Robert R., Jr.

CORPORATE SOURCE: Div. Pharm. Sci., SmithKline Beecham Pharm., King of
Prussia, PA, 19406, USA

SOURCE: Expert Opinion on Investigational Drugs (1997), 6(4),
367-387

CODEN: EOIDER; ISSN: 0967-8298

PUBLISHER: Ashley Publications

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A **review**, with 166 refs. The cloning of multiple subtypes of
both **alpha.1-** and **alpha.2**-adrenoceptors has renewed
interest in the therapeutic application of agents interacting with these
receptors. Effort has primarily been directed towards the design
of uroselective **alpha.1**-adrenoceptor antagonists for the
treatment of benign prostatic hyperplasia (BPH). Evidence is
accumulating
for the involvement of a novel **alpha.1**-adrenoceptor, designated
as **alpha.1L**-adrenoceptor, in **alpha**
.1-adrenoceptor-mediated smooth muscle contraction in prostatic and other
urogenital tissues. While several antagonists showing a high degree of
uroselectivity in animal models have been identified, their clin.
superiority over the currently available **alpha.1**-adrenoceptor
antagonists has not yet been demonstrated. It is possible that the
interaction with **alpha.1**-adrenoceptors, as yet uncharacterized
subtypes, at nonprostatic sites contributes to the therapeutic activity
of
this drug class in BPH. The **alpha.1**-adrenoceptor subtypes
involved in the control of vascular tone are currently being evaluated,
and the profile of interaction with the various **alpha**
.1-adrenoceptor subtypes may play a key role in the efficacy of
cardiovascular drugs such as carvedilol. **alpha.2**-Adrenoceptor
agonists are now being employed for a variety of therapeutic
applications,
most involving actions on **receptors** with the central nervous
system (**CNS**). These agents are useful in the treatment of
hypertension, glaucoma, opiate withdrawal and attention deficit
hyperactivity disorder (ADHD), and as analgesics and adjuncts to general
anesthesia. While subtype selectivity has not yet been applied to the
design of new **alpha.2**-adrenoceptor agonists for these
applications, recent gene mutation/knock-out expts. have identified the .
alpha.2-subtypes involved in some of these actions, and
optimization of a therapeutic profile may be possible. Furthermore, the
design of agents combining affinities for multiple adrenoceptor subtypes,
or the combination of a specific adrenoceptor affinity profile with
another pharmacol. action, may offer advantages over mols. selective for
an individual adrenoceptor subtype.

L9 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1997:65995 CAPLUS

DOCUMENT NUMBER: 126:113272

TITLE: Role of prostaglandins in the stimulation of the hypothalamic-pituitary-adrenal axis by **adrenergic** and neurohormone systems

AUTHOR(S): Bugajski, J.

CORPORATE SOURCE: Institute Pharmacology, Polish Academy Sciences, Krakow, Pol.

SOURCE: Journal of Physiology and Pharmacology (1996), 47(4), 559-575

CODEN: JPHPEI; ISSN: 0867-5910

PUBLISHER: Polish Physiological Society

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A **review** with 78 refs. Role of prostaglandins (PGs) in the activation of the hypothalamic-pituitary-adrenal (HPA) axis by the **adrenergic** agonists, ACTH-releasing hormone (CRH) and vasopressin (VP) in rats under basal and social stress conditions was investigated. Systemic or intracerebroventricular (icv) pretreatment with indomethacin powerfully reduced the corticosterone response to icv phenylephrine, an **.alpha.1-receptor** agonist, significantly diminished the response to clonidine, an **.alpha.2-receptor** agonist, but did not alter the response to isoprenaline, a **.beta.-adrenergic** agonist. Consequently, indomethacin considerably reduced the corticosterone response to noradrenaline, an **.alpha.1-** and **.alpha.2-adrenergic** agonist, but did not change the response to adrenaline, a predominant **.beta.-adrenergic** agonist. Thus, prostaglandins considerably mediate the HPA activity stimulated via central **.alpha.1-** and **.alpha.2-** but not **.beta.-adrenergic receptors**. Social crowding stress for 3 days did not affect the corticosterone response to i.p. or icv CRH, but drastically reduced the response to VP. In stressed rats indomethacin did not alter the corticosterone response to CRH but significantly further impaired the diminished by stress corticosterone response to VP. Neither social stress nor endogenous prostaglandins affected the responsiveness of the CRH system. By contrast, both social stress and prostaglandins considerably diminished the HPA response to VP. The above results indicate that both these neurohormone systems have a distinct mode of adaptation and interaction with PG systems during social stress. Interleukins, particularly IL-1 β and IL-6, activate the HPA axis. Most immunol. stimuli and interleukins also activate both the central and the peripheral noradrenergic systems. Activation of the HPA axis in vivo depends on the secretion of CRH, an intact pituitary and the ventral **adrenergic** bundle innervating the hypothalamic paraventricular nucleus. Interleukins may cross the blood-brain-barrier or be produced in the **CNS** to stimulate their **receptors** in brain structures involved in the regulation of the HPA axis.

L9 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2002 ACS

L9 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1992:400953 CAPLUS
 DOCUMENT NUMBER: 117:953
 TITLE: Electrophysiological consequences of activation of
 adrenoceptors in the **CNS**
 AUTHOR(S): McCormick, David A.
 CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, USA
 SOURCE: Adrenoceptors: Struct., Mech., Funct., [Proc.
 Manchester Symp. Pharmacol. Adrenoceptors], 3rd
 (1991)
 , Meeting Date 1990, 159-69. Editor(s): Szabadi,
 Elmer; Bradshaw, Christopher M. Birkhaeuser: Basel,
 Switz.
 CODEN: 57QSAA
 DOCUMENT TYPE: Conference; General Review
 LANGUAGE: English
 AB A **review**, with 30 refs., on the electrophysiol. consequences of
 activation of **.alpha.1-**, **.alpha.2-**, and
.beta.-adrenoceptors in the central nervous system (**CNS**).

L9 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1983:516128 CAPLUS

DOCUMENT NUMBER: 99:116128

TITLE: The physiological role of **.alpha**
.-adrenoceptors in the **CNS**: new concepts
from single-cell studies

AUTHOR(S): Aghajanian, G. K.; Rogawski, M. A.

CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, 06508, USA

SOURCE: Trends Pharmacol. Sci. (1983), 4(7), 315-17

CODEN: TPHSDY; ISSN: 0165-6147

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A **review** with 10 refs., on the synaptic localization and
functional classification of **.alpha.1-** and **.alpha.2-**
adrenergic receptors in the central nervous system.